THE SCIENCE AND PRACTICE OF SURGERY

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EIGHTH EDITION

With 820 Illustrations

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Dedicated

To our Friend and Teacher

the late

SIR GEORGE MAKINS, G.C.M.G., C.B.

In Tribute to a Great Man

PREFACE TO THE EIGHTH EDITION

In producing this eighth edition the authors confidently hope that it will receive as kind a welcome as its predecessors. The considerable delay between the seventh and eighth editions has been caused by a continuance of the wartime restrictions on printing and the difficulties of obtaining paper.

It has been suggested that the scope of this work should be altered so that it would deal only with the bare physical signs and one method of treatment for each condition mentioned, but we have resisted this suggestion for we feel most strongly that the medical student's knowledge must be built on a broad foundation so as to enable him to diagnose and treat his patients' ailments ably and efficiently. We feel sure that our intelligent readers and their teachers will agree with our contention.

Owing to the difficulties alluded to, we have had to modify considerably the contents of these two volumes and most regrettably have been forced to omit Mr. Gimblett's valuable chapter on Diseases of the Eye.

The whole work has been thoroughly revised and brought up to date, many parts of it being re-written. There are additional chapters on Plastic Surgery by Mr. R. J. V. Battle; and X-ray Therapy by Dr. J. A. C. Fleming, while Dr. J. W. McLaren has re-written the chapter on X-ray diagnosis; Dr. A. F. Potter has thoroughly revised and modernised the chapter on Anæsthetics, and Dr. T. Anwyl Davies has brought the sections on Venereal Disease into line with present-day treatment. Recent progress in the field of chemotherapy has been recorded in some detail, together with notes on Penicillin and Streptomycin. Each volume is now indexed separately.

In addition, largely owing to the war experiences of one of the authors, we have been able to amplify the surgical aspects of those tropical diseases met with in the Middle East, Africa and India, from which countries we welcome so many readers. We hope that this section of the work may prove of especial value to them.

We are indebted to the Medical Faculties of the Witwatersrand University, Johannesburg; the Fouad 1st University, Cairo; Farouk University, Alexandria; the Royal University, Baghdad and American University, Beirut, the Kitchener Medical College, Khartoum, and the Hospital for Sick Children, Gt. Ormond Street, for co-operation and illustrations. We are further grateful to colleagues in many lands and especially to Professor Nagib Makar, F.R.C.S., of the Kasr el Aini Hospital, Cairo, for assistance and helpful criticism in the preparation of this edition

Finally we must thank the publishers, and especially Mr. J. Rivers, for their great help and co-operation which has enabled this work to be produced in very difficult conditions

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P. H. M.

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THE SCIENCE AND PRACTICE OF SURGERY

CHAPTER I

GENERAL SURGICAL PROCEDURES

Examination of a surgical patient—Asepsis and antisepsis—Technique in operative surgery—Preparation of patients for operation—After-treatment of operation cases—Post-operative complications, their diagnosis and treatment.

Examination of a Patient. The inclusion in a surgical text-book of all diseases is both undesirable and impossible, and in this volume an attempt

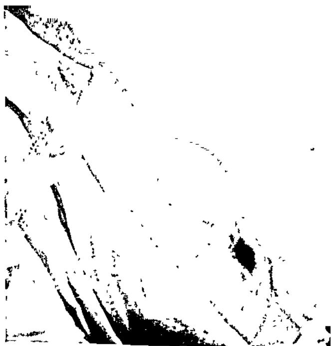


FIG. 1. Fibro-adenoma of the breast, visible on inspection. The overlying skin is normal and not puckered, showing that it is not a carcinoma. The definition of the edges eliminates an inflammatory origin.

has been made to indicate to the would-be surgeon, lucidly and briefly, the urgical conditions which he may be called upon to investigate during his areer, and to outline not only the physical signs and symptoms by which the

case can be diagnosed, but also the pathological conditions from which these signs result, and, moreover, to indicate on what lines treatment may be undertaken for the amelioration of the patient's condition. But it must be understood that a detailed explanation of the points of differential diagnosis between these various diseases is out of place in a text-book of general surgery, and to ascertain both these and the full description of clinical methods used in their investigation, the reader is referred to special text-books on these subjects.

Below is given a brief scheme indicative of the general lines on which a patient should be approached and his case investigated.

The first question that a student of surgery, or for that matter a surgeon, has to ask himself on being confronted with a sick patient is as to the cause of the trouble. "Is this lesion due to trauma, infection, or new growth?" And it is on the accurate answer to this query that the life of the patient, and incidentally the success of the practitioner, frequently may depend. It cannot be impressed too strongly on the medical student that nearly all disease is due to one of these three causes, *trauma*, *infection* or *new growth*, and that the exact cause can be elicited only in the majority of cases after a careful and systematic examination not only of the local condition, but of the whole body of the patient. It is necessary that the bearing and conduct of the surgeon should convince the patient of his interest and sympathy, and so win complete confidence.

Turning to the examination itself, this should be conducted gently and with due regard to the patient's feelings and comfort, the attention of the patient being held meanwhile by obtaining a *detailed history of the case*, which is always of the utmost value.

The following routine should be followed in every case:—

1. *Inspection*, both local and general, is of the greatest value, and should be made in a good light without being too close to the patient.

2. *Palpation* of the local lesion and its immediate area should be carried out next in order to ascertain the shape, consistency, attachments and limits of the local condition. Similar examination of distant parts may be indicated.

3. *Percussion* may be necessary locally.

4. *Auscultation* may be necessary locally in a few cases. Both of these are essential in *the examination of the cardiac and respiratory systems and the abdomen*, which should be carried out as a routine in all cases.

5. *Examination of the urine* is an essential part of the investigation of a case, as is also the examination of the *central nervous system*.

Rectal or pelvic examination should be made in all cases of abdominal diseases.

It will be seen from the foregoing that the surgeon must of necessity be a physician also if he is to give to his patients that thorough preliminary examination which alone can justify his confidently recommending resource to the knife as the only certain means of cure of the condition on which his opinion is sought.

Asepsis and Antisepsis. As will be explained, sepsis results from the infection of the tissues by micro-organisms (Chapter III.), and in order to prevent such a calamity resulting during operations very stringent precautions have to be taken by all parties concerned. On those accustomed to the orderly quiet and cleanliness of the modern operating theatre it is difficult to impress the necessity for routine measures, which are essential to prevent a return of the virulent post-operative suppuration which was all too

frequent in the days before Lord Lister, by the introduction of antiseptics into surgery, inhibited the growth of the bacteria which Pasteur had shown to be the cause of infection in operation wounds; but upon those who saw something of the surgical conditions prevailing in the field during war that necessity was impressed in a forceful and dramatic manner, and with it came the realisation of how very necessary is the attainment of those essential precautions against infection, and how very simple they need be to be effectual in actually excluding organisms; whereas, once these have gained admission to the tissues, it is almost impossible to eliminate them or even effectually inhibit their growth.

Asepsis aims at the exclusion of all micro-organisms from the wounds by the use of dressings and instruments sterilised by heat, usually in the form of boiling water or steam, and by the thorough cleansing of the skin of the patient, surgeons and assistants.



Fig 2. An Aseptic Operating Theatre.

Antisepsis aims at the destruction of the organisms, or at least the inhibition of their growth, after they have gained access to the operation area, by the use of chemical substances known as antiseptics.

Inasmuch as these antiseptic substances frequently can be used only in strength sufficient to inhibit the growth of the bacteria, and as even in this strength they exert an irritant action on the tissue cells, which in greater concentration they destroy, the aseptic method is preferable in practice, as here nothing is employed to damage tissue cells and impede repair, organisms are excluded, and no misplaced faith is given to the uncertain action of chemical substances on their growth.

The majority of surgeons nowadays rely, therefore, on sterilisation by som[e] form of heat to exclude organisms from instruments and dressings[;] inasmuch as this method cannot be used in cleansing the skin of ei[ther] surgeon or the patient, antiseptics in various forms have to be r[...]

anti-

this purpose. Moreover, although experience has shown that sterile isotonic saline is by far the least harmful lotion to apply to cut surfaces, and that it can be used safely under all conditions, yet there are many surgeons who prefer weak antiseptic lotions for this purpose, and a list of the various lotions in common use is appended.

Sterile normal saline solution is approximately isotonic with the blood plasma, and therefore may be employed with impunity at or slightly above body temperature (100°–115° F.), as it exerts no irritating or devitalising effect on the tissue cells. It is prepared by dissolving sodium chloride in water in the proportion of 1 drachm of the salt to each pint of water; the whole must be sterilised by boiling and then allowed to cool, or else cooled by adding cold sterile saline. This lotion always should be used for moistening the peritoneum of exposed bowel, in skin grafting, etc., and may be employed with great advantage as a hand lotion throughout the whole operation; this, indeed, is the practice of most surgeons of the aseptic school.

Sterile water is also non-irritant, but not being isotonic with the tissues, it causes osmosis from these, and is therefore not so good as normal saline. Like saline, it should be employed at or just above body temperature, but if used as a hæmostatic it should, like saline, be at a temperature of from 125°–135° F

Sterile paraffin and **glycerine** are non-irritant lubricants and may be used to lubricate instruments for their passage through mucous canals, *i.e.*, catheters, cystoscopes, sigmoidoscopes, etc., or as a dressing to raw and granulating wounds, where they prevent the gauze adhering to the delicate tissues and so stop damage when the dressing is stripped off.

Alcohol employed as 70 per cent. spirit solution is a valuable antiseptic, and on its use probably depends the efficacy of the various alcoholic solutions employed in sterilising the skin of the patient and surgeon. It should be in contact with the surface for at least five minutes, and to be efficient must be applied to the *dry* skin. If used for sterilising phials of catgut, scalpels, etc., these should be immersed at least half an hour before use.

Biniodide of mercury in alcoholic solution is the most popular and probably the most efficient antiseptic lotion in general use. It is a powerful germicide, does not tarnish instruments, and as it does not react much with albumen, can penetrate the tissues more thoroughly than those salts which coagulate albumen and so form a film on the surface of the wound, which prevents the antiseptic penetrating efficiently into the tissues; this is the case with perchloride and other mercurial salts, picric acid, and to some extent carbolic. If used for application to the tissues, the aqueous solution (1–1,000) is less irritating and more efficient in penetrating power than the more expensive alcoholic variety.

Iodine solution, usually employed to sterilise the skin in the form of the tincture ($2\frac{1}{2}$ per cent. in alcohol), is an efficient but irritating antiseptic, and its application to wounds is painful, though it is commonly employed as a first aid dressing in factories, etc. Like all alcoholic antiseptic solutions, it must be applied to a dry surface to be efficient. A 1 per cent. solution in potassium iodide is used in the sterilisation of catgut sutures and ligatures.

of skin preparation is unsuited for the face and neck

A 1 per cent. aqueous solution is of some value as a first dressing for burns and scalds (Chapter IV., p. 61). Occasionally both the above antiseptics give rise to toxic rashes of an erythematous type which may resemble scarlet fever, but cause intense irritation and may be followed by extensive desquamation.

Perchloride of mercury in a 1-500 or 1-1,000 aqueous solution was a very popular antiseptic, but is more toxic and is not so efficient as biniodide, which has largely superseded it, and which, in addition, has the advantage of not tarnishing instruments. Like most mercury salts, it combines with steel and silver, and therefore must not be brought in contact with instruments.

Carbolic acid is the oldest of the antiseptics of the modern school, having been popularised by Lord Lister. It is, however, of poor germicidal power when compared with other antiseptics, and though it undoubtedly inhibits the growth of most micro-organisms if left in contact with them for long periods, yet in solutions strong enough to ensure this (1-20) it is both toxic to the tissues and even to the individual; for it may produce both gangrene, especially of fingers and toes, and nephritis, the urine in this latter case being green in colour and the patient showing signs of toxæmia, such as breathlessness and a rapid weak pulse.

The 1-20 solution is, however, valuable for the storing of sterile ligatures to prevent organisms gaining access, though it undoubtedly tends to rot the fabric. Pure carbolic is a potent antiseptic which deliquesces, and is locally anæsthetic if applied to the tissues, in which it causes a painless superficial necrosis, the area being covered with a white slough.

Liquor sodae chlorinatae and **Eusol** are excellent for cleansing sloughs from foul wounds, but inasmuch as the hyperchlorous acid and chlorine, on which their efficacy as cleansing agents depends, destroy epithelium, they must be discontinued as soon as the wound is clean or they prevent healing.

Camphenol is a powerful antiseptic prepared by mixing pure carbolic and camphor in equal parts, when these deliquesce and produce an oily greenish liquid; it is of value in dressing large septic wounds, where a painless dressing and stoppage of absorption by superficial necrosis of tissue are desired, as in carbuncles when the sloughs have been removed.

Hydrogen peroxide, usually used in a solution giving off 10 volumes of nascent oxygen when in contact with organic matter, is a valuable antiseptic in dealing with anaerobic micro-organisms. It also cleanses wounds by its mechanical action when bubbling off oxygen. It is not suitable for use in closed cavities, as it distends these and may strip up the surrounding tissues and convey infection to the deeper parts. It is valuable as a styptic and in loosening blood-soaked dressings. The water left after the oxygen has bubbled off should be cleaned away from the wound.

Formalin. A 40 per cent. aqueous solution of formaldehyde is a powerful antiseptic, and if applied in this strength produces immediate death of tissue with a black slough. It is sometimes thus used to cleanse the surface of septic wounds. It is more usually employed as a solution of a strength of about 4 per cent., but is very irritant and pungent. The vapour is used for disinfecting rooms and sterilising cystoscopes and catheters.

Flavine and **Acriflavine**, 1-1,000 in alcoholic solution, are powerful and non-irritant germicides, much used in dressing septic wounds.

Lysol (1 or 2 per cent.), **Creolin**, **Izal**, **Cyllin**, **Dettol**, are all coal-tar derivatives, of which the most used is lysol; this, being derived from the action of [illegible] be used for its soapy properties as well as an anti-

septic. Pure lysol is valuable for keeping knives in, as it neither rusts nor blunts them, and many surgeons use it for sterilising scalpels; it has, however. the disadvantage that it renders them slippery.

Sources of Infection. It is now generally conceded that infection of all operation, and for that matter other wounds, is the result of invasion by micro-organisms from some "outside" source, it being understood that the term "outside" includes the cutaneous and mucous surfaces, *i.e*, the free surfaces which are not normally in contact with the tissues, and are, moreover, covered with micro-organisms. As a matter of fact, "auto-infection" from the skin is of rare occurrence, presumably due to an acquired immunity from the toxins of these organisms continually being absorbed into the system, and though it should be carefully guarded against at operations, auto-infection from skin surfaces is not a matter of great import.

Very different, however, is the danger of infection from other "outside" sources, and before discussing the methods used in combating these it will be well to consider briefly the possible sources of such infection. These are:—

1 The skin of the surgeon and his assistants, where, in the fissures and glands, numerous micro-organisms are present which it is almost impossible efficiently to dislodge. The mucous membranes of the mouth and nose must not be forgotten as sources of infection.

2 The skin and mucous membranes of the patient have already been mentioned, but especial care must be taken to exclude infection in those cases where the intestinal tract is opened during operation.

3. The clothing of the surgeon, assistants and patient are potent sources of infection, and for this reason as much as possible should be removed before entering the operating theatre, and the remainder covered by an overall of washable and easily sterilised material The same applies to bedclothes.

4. Instruments, trolleys, tables, basins, etc., should be of glass or metal and capable of being sterilised by heat.

5. Sutures, ligatures and dressings must be capable of ready sterilisation, if possible by heat.

6. Saline solutions or antiseptic lotions used for applying to the wound surfaces must be sterile, and so need to be prepared from boiling or freshly-boiled water.

7. The air, which was at one time thought to be a potent source of infection, is now known to be little likely to convey micro-organisms to the wound in an operating theatre, provided it is still. Draughts, dust, undue movement or talking should be avoided in operating theatres, and similarly in emergency operations in private houses no hasty cleaning and rearranging of the furniture should be permitted in the room where an operation is to take place.

8. All wounds other than those inflicted by the surgeon's knife in the course of an operation must be regarded as infected by micro-organisms, and therefore need careful cleansing. Should there be any suspicion of fouling with road dirt or soil, antitoxic sera should be administered as a routine against tetanus (p. 90) and gas gangrene (p. 169).

STERILISATION

Heat is by far the most efficient sterilising agent at our command.

(1) *Moist heat* is usually employed, either in the form of (*a*) boiling water or (*b*) of steam circulating under pressure, as this is more efficient than (2) *dry heat*, which can be used in the form of (*a*) an actual fire flame, (*b*) the cautery, or (*c*) an oven.

Sterilisation by steam circulating under pressure is best carried out in a double-jacket steriliser, such as that of Schimmelbusch, or some modification of the Washington-Lyons apparatus; these need to be placed in a special chamber and carefully tended. Dressings, overalls, and other appliances not damaged by steam are loosely packed in drums or tins and covered with a layer of wool, the lid being left open. The steriliser is then closed and a 10-inch vacuum established to exhaust air from the dressings, etc., and so enable the steam to penetrate; in ten minutes steam under 15 lbs. pressure is admitted, and kept circulating for twenty minutes, when it is shut off and a 15-inch vacuum established to dry the steam from the dressings, and maintained for twenty minutes, when the steriliser is opened and the tins

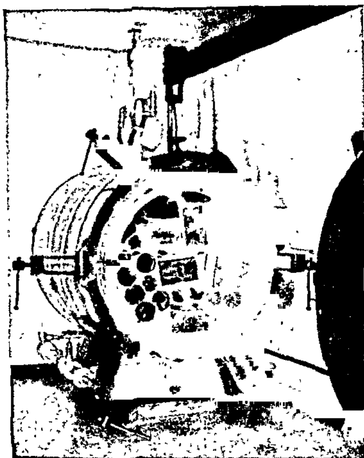


FIG. 3 Steam Steriliser—front removed to show dressings *in situ*.

removed, closed, and sealed. Leather must never be placed in steam sterilisers, as it is thereby destroyed.

Boiling in water or oil is carried out in some form of fish-kettle steriliser, the instruments or ligatures to be boiled being contained in a wire tray which can be lifted out. The steriliser lid must be closed during boiling, which should last for from five to fifteen minutes, the water boiling actively, and even this is not sufficient to kill all spores of bacteria, such as anthrax, *B. welchii*, etc. Rubber materials may be boiled, but care must be taken that instruments are not boiled at the same time as gloves, as these tend to be perforated or torn.

Gum-elastic instruments, catgut and kangaroo tendon are destroyed by boiling

Flaming is an efficient but costly method of sterilising bowls or cutting instruments, which must be held in forceps, dipped in alcohol or ether, and then fired. Care must be taken not to ignite surrounding dressings or objects and not to fire the reservoir of alcohol or ether, which must be covered before the flaming is attempted.

The actual cautery or diathermy cautery is sometimes used, as in cutting across bowel, to secure a sterile surface beyond the clamps, or to ensure hæmostasis.

These agents will be employed in every case possible, and, if efficient methods are used, are absolutely safe to destroy all micro-organisms, but it must be understood clearly that *unless things so sterilised are subsequently protected*, as by inclusion in a hermetically sealed tin, *reinfection will occur.*

There are, unfortunately, certain substances, such as the human body and ligatures derived from animal sources, such as catgut, kangaroo tendon, etc., which are destroyed by heat at a sufficient temperature to ensure sterilisation, and one is therefore forced to rely on other and less efficient methods for the removal of micro-organisms from the skin of the patient and surgeon, and from animal ligatures; here, indeed, antiseptics must be employed for this purpose, which in the case of the skin are ably aided by the mechanical removal caused by washing, especially if this is carried out under running water.

The various methods of sterilisation by heat and the antiseptic lotions in common use have been described, and need no further discussion here, but it is proposed to indicate briefly how the elimination of the various sources of infection in the operating theatre is carried out.

1. **The surgeon's and assistant's hands and arms** need careful attention at all times, and not only just prior to operations. In this respect always *remember never to touch pus with ungloved fingers* and to remove all dressings with forceps. The skin must be kept smooth and occupations which lead to cracking and fissuring of the epidermis avoided; especial attention must be paid to the nails, which need regular paring and cleaning. The hair should be kept short and covered with *a sterile linen cap* during operations. The teeth need regular attention, but the elaborate oral toilette performed by some Continental surgeons before operations is unnecessary. During operations *and dressing of wounds a thick gauze veil should be worn* over the mouth and nose to prevent drops of saliva falling on the operation area

The outer clothing of the surgeon and his assistants should be removed before entering the operating theatre, and may with advantage be replaced by light overalls of duck, or by flannels, kept in the theatre and washed frequently. In many cases, however, the surgeon contents himself with

Before each operation and after washing, the surgeon dons a sterilised linen overall, which covers all clothing and may have long sleeves, which are tucked into the gloves, or short ones coming to the elbow. In either case the hands should be washed again before putting on the gloves, and it is wise to regard the overall as surgically unclean once it has been donned, as it touches the tables, sinks, etc., and this may escape notice, as it fits loosely. This gown should be changed between each operation

Immediately prior to an operation some surgeons take a complete bath, but this is hardly necessary, and most are content to wash the hands and forearms thoroughly in soap and running water for at least five minutes, special care being given to the folds around the nails. The soap should be applied to the almost dry skin and worked up into a lather, and then washed off, this process being frequently repeated. Many surgeons then immerse the hands in a solution of antiseptic, such as biniodide of mercury or spirit, but we do not consider this necessary if the washing has been adequate, as the soap is a good antiseptic and, moreover, does not roughen the skin like most antiseptic solutions. After this, *sterile rubber gloves* should be put on; these may be "wet," *i.e.*, sterilised by boiling in water, or, better, "dry," sterilised by steam; in either case they should be worn as a routine for every operation, and also for dressing all septic cases. In donning them great care should be taken never to smooth down one glove with the bare hand before both have been put on, otherwise organisms may be carried to the outside of the glove by the bare skin of the other hand. Should "wet" gloves be used, care must be taken that water from the inside does not run over the glove as it is being put on, and a strip of sterile muslin should be applied to the wrist around or inside the cuff of the glove to prevent water from inside, which will contain organisms from the skin, being squeezed out during the conduct of the operation.

2. **Ligatures and sutures** fall into two classes: (1) the absorbable animal tissues, of which the chief is catgut; (2) non-absorbable silk, thread, wire, etc.,

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strong and flexible, (3) be absorbable if possible, so as to avoid irritation in the tissues, but not before its purpose is fulfilled.

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stored. It is doubtful whether spores in silk or thread can be killed by prolonged boiling. Care must be taken that the edges of ligature jars are protected by a sterile towel or boiled metal collar.

Thread is prepared in the same manner as silk.

Horsehair is washed in soap and water, boiled for three minutes, and kept in 1–20 carbolic for two weeks before using.

Silkworm gut, Nylon, and Japanese Salmon gut (which is prepared from the fibres of certain seaweeds) are boiled for five minutes and kept in 1–20 carbolic or spirit; the finer varieties may be boiled for three minutes.

Catgut. (*a*) *Iodised Catgut.* The raw catgut should be soaked in ether for forty-eight hours to remove the fat. It is then loosely wound on slats and immersed in iodine solution (1 per cent. iodine and 1 per cent. potassium iodide in water) for eight days, when it is ready for use. Any catgut left over

period.

(*c*) *Van Horn's Catgut.* The sealed glass tubes can be boiled for five minutes before use, and may be broken open on the instrument table when required.

(*d*) *Luken's Catgut* (simple, iodised or tanned). The sealed glass tubes are soaked in spirit or 1-20 carbolic for thirty minutes before use.

(*e*) *London Hospital Catgut* (plain or chromic). This is immersed in iodine solution for eight days as above.

Gold leaf can be boiled gently for five minutes.

Kangaroo tendon is used in the same way as Luken's catgut.

3. Sterilisation of Instruments. All blunt metal instruments should be sterilised by boiling for at least five minutes in water to which 1 per cent. sodium bicarbonate has been added. This serves the purpose of removing grease, stopping discoloration, and raising the temperature of the boiling water about 5° C (*i.e.*, to 105° C.). The instruments are then cooled and placed on a sterile cloth or in a tray of sterile saline on the instrument table.

Cutting instruments may best be sterilised by being wrapped in gauze and boiled for one minute, and subsequently immersed in spirit for twenty minutes before use. Some surgeons, however, prefer keeping scalpels in spirit, pure lysol or carbolic for at least twenty-four hours before use instead of boiling. Rubber tubing and catheters, glass tubing, nozzles, syringes, etc., should be boiled for five minutes If they are required to be kept sterile for a long period, they can, after boiling, be put in 1–100 formalin, 1–20 carbolic, or lysol-ether solution, but need well washing in sterile water before use.

Cystoscopes and ordinary gum-elastic instruments (catheters and bougies) must be washed carefully in soap and water, thoroughly rinsed, then washed with methylated spirit and finally dried. Before use they are sterilised best in the formalin-vapour steriliser or by immersion in methylated spirit or 1 in 20 carbolic for thirty minutes.

Grey gum-elastic catheters (ureteric or urethral) may be boiled for three minutes in long muslin bags, with a separate compartment for each catheter. The catheters must on no account come into contact with each other or with the steriliser when being boiled. After use they are washed under a powerful stream of hot water, syringed out with spirit, and then dried.

Radium must not be boiled ; the filter or outer tube can be boiled for five minutes Certain varieties of radium needles are boilable.

A useful *sterilising solution* in which to keep needles, cutting instruments (and other instruments for emergency use), and which neither rusts nor blunts them, is

℞	Lysol	℥i.
	Surgical Spirit	Oi.

Immersion for at least half an hour is necessary to ensure sterilisation.

In instances where instruments have been used for cases such as *anthrax*, *tetanus*, or *gas gangrene*, where the causative micro-organism is spore-forming, all instruments need sterilising in the high-pressure steam apparatus ; dressings, ligatures, etc , should be burned.

4. Bowls and basins should be sterilised in the steam apparatus or boiled. If this is not practicable, they may be " flamed " by washing the inside with spirit and " firing " it. This method is not [illegible]

[illegible]

washed over with spirit or 1–20 carbolic before operation. Overalls, towels, dressings, swabs, etc., should be packed lightly in tins and sterilised for [illegible]

unless reasons of economy demand otherwise, when they are washed and re-sterilised. If this is impracticable boiling may be resorted to, and the towels or dressings used wet, care being taken not to scald the patient.

Marine sponges are not often employed, but if used should be washed in ether soap and water, then immersed for twelve hours in sulphurous acid, 1 part to 10 of water and then washed in sterile water.

PREPARATION OF THE PATIENT

The patient should enter the institution at least twenty-four hours before operation, when possible, so as to become accustomed to the surroundings, routine, etc. Previously to this the teeth should have been put in order and the bowels well regulated. In cases where special feeding apparatus is to be used after operation, as in tongue cases, the patient should be practised in its use.

The diet should be light, but except in cases of operation on the rectum no special purgation or enemata are necessary provided the bowels are acting regularly. Large amounts of sugar are advantageous before an operation.

It is essential to explain to the patient the nature and results of the intended operation, but at the same time not unduly to alarm him or to make him regard the operation as anything but a stage in the treatment of his disease. It is very necessary to secure a good night immediately preceding operation, and should the patient be nervous or wakeful a sleeping draught should be given, or morphia may be administered.

The *operation area* should be shaved on admission, and the patient take a bath then and on the morning of operation. The skin in the area is prepared both on the morning of operation and again in the theatre by one of the following methods :—

1. Washing with soap and water for five minutes on both occasions.

2. Washing with soap and water on the first occasion, and applying ether or spirit to the dry skin in the theatre.

3. Painting the dry skin on both occasions with either 2 per cent. iodine in rectified spirit or 1 per cent. picric acid in spirit. Some surgeons prefer plain spirit to which methylene blue is added as a colouring agent, to demark the cleaned area, while others use brilliant green 1 per cent. alcoholic solution, or ether. Between the first and second occasions the area is in all cases covered with a sterile dressing.

The patient may be given an injection of atropin sulphate, gr. $\frac{1}{100}$, or this combined with morphia, gr. $\frac{1}{4}$, and scopolamine, gr. $\frac{1}{200}$, half an hour before operation; he should be conveyed to the theatre warmly wrapped and be anæsthetised outside the actual operating room. In the theatre the blankets should be removed and warmed bath towelling substituted as a covering to maintain body warmth. The operation area is exposed, packed around with sterile mackintoshes, cleaned, and the whole covered with sterile towels.

It is out of place to discuss *operative procedure* here, but a few essential points may be mentioned.

1. Make an adequate skin incision, and cut cleanly and boldly, keeping the incision to its full length throughout its depth. Never scratch and tear, for this causes damage to tissue and increases its liability to infection. Remember that there are three kinds of operators : slashers, scratchers, and surgeons

2. Secure adequate hæmostasis and disarrange tissues as little as possible.

3. Protect exposed tissues by enveloping them in gauze soaked in warm saline, and by covering exposed skin by clipping towels to the wound edges

4. Don't put your fingers or hands into the wound; use forceps and retractors

5. Close the wound up carefully by one of the methods indicated in Chapter IV., p. 43, remembering that it is essential to approximate the deeper tissues in order to prevent hæmatomata and subsequent stretching of the scar.

AFTER-TREATMENT OF OPERATION CASES

The patient should be covered up warmly and conveyed back to a warm bed, care being taken to protect him from draughts by covering the head during transit from the theatre to the ward in order to lessen the chances of post-anæsthetic pulmonary troubles.

It is often advisable to administer morphia, gr. ¼, at once in order to combat collapse, or because it is desirable to keep the patient quiet until the effects of the anæsthetic have passed off. Luminal gr. iii intramuscularly will be found useful.

A careful watch must be kept to see that the patient does not swallow his tongue, or do himself any harm by flinging himself about, and that he does not choke or befoul himself if he vomits.

It is important to reassure the patient as soon as he is even semi-conscious, and, in order to secure the rest and tranquillity of mind which are essential, morphia may be given freely for the first twenty-four hours.

All wounds should be re-dressed at the end of twenty-four hours, as there is usually a slight oozing and, apart from the caked blood clot being a source of discomfort to the patient, it is an excellent pabulum for the growth of skin bacteria.

If the wound is clean it needs no further dressing until the metal clips (fourth day) or stitches (eighth day) are removed, unless a rising temperature or pain suggest suppuration, which is usually manifest on the third or fourth day after operation, but may be delayed as late as the tenth in cases of deep suppuration.

Where a drainage tube is present daily dressings are necessary, which continue till the tube is removed, usually on the second or third day after operation. Discharging wounds may need dressing several times in the twenty-four hours.

After removal of stitches or clips, wounds, if healed, need no protection, and, indeed, some surgeons do not apply any dressing after operation other than a piece of gauze laid over the wound. Hernia wounds and similar clean cases do well under this treatment, but they lack the support which a firm bandage, elastoplast or strapping gives.

The patient should be [illegible]

and may prevent complications, such as pulmonary embolus. Ordinary straightforward cases, such as herniæ in young people and quiescent appendices, should be allowed out of bed as soon as possible, usually when the clips or stitches have been removed, although as a general rule abdominal cases are kept in bed quite ten days; but patients after operations on the mouth, face and breast are got out of bed within [illegible]

for a more prolonged period.

The diet of a patient after operation should be light, but consist of dry and solid food as well as liquids, large quantities of which [illegible]

flatulence and tend to make the patient vomit and suffer from abdominal discomfort. There is no need to withhold food in the days immediately succeeding operation if the patient desires it, but in cases of operation on the stomach or upper part of jejunum this must be selected judiciously and given in small quantities.

As a general rule the diet for the first twenty-four hours after operation should consist of tea, lemonade, Bovril or any other fluid fancied (but large amounts of aerated waters and milk are to be avoided as causing distension), and biscuits, toast, jellies, etc. After this the diet can be increased in any way the patient fancies, up to fish and chicken ; large quantities of green vegetables and pastry should be avoided, especially in cases of abdominal operations. Meat may be eaten at the end of a week. Alcohol should be given to old people and those accustomed to its daily use.

After an operation such as a *gastro-enterostomy*, the diet for the first twenty-four hours should consist of sips of water, diluted tea or black coffee, jelly and Bovril or clear soup (milk should be avoided for the first three or four days, as it forms septic clots on and around the operation site).

On the second and third days the diet may be increased by adding biscuits, toast, lightly-boiled eggs, etc., which must be thoroughly chewed up.

On the fourth day boiled and fried fish and boiled potato may be partaken of, and milk may be given if desired.

On the sixth day chicken, and on the tenth day mutton, may be taken, and ordinary diet, carefully masticated, thereafter resumed with perfect comfort and safety to the patient.

The *bowels* should be opened on the second or third night after operation by the administration of a brisk purge, such as Mist. Sennæ Co. ℥i, Cascara Evacuant ʒii or Ol. Ric. ℥ss or ℥i, except in the case of :—

1. *Acute inflammation of the intestinal tract*, when purgation should be avoided for as long as a week, especially if peritonitis is present. In these cases distension may be controlled by injections of pituitrin, $\frac{1}{2}$ to 1 c.c., given once or twice a day ; injections of eserine sulphate, gr. $\frac{1}{70}$ to $\frac{1}{100}$ six-hourly or acetyl-choline $\frac{1}{2}$ to 1 c.c. four-hourly, will also help. Turpentine and ox bile enemata are useful (see Vol. II., Chapter XV.)

2. *Rectal cases*, *e.g.*, hæmorrhoids, when a purge should be given the night following operation.

3. *Gastric and duodenal cases*, where enemata are preferable for the first four or five days, if the bowels are not opened naturally.

Post-anæsthetic vomiting (see Vol I., Chapter XXVI.) is an all too frequent sequel to operations, but can hardly be called a complication and usually ceases after the first twelve hours. Should it persist, however, it may cause inconvenience, and often can be cured by the administration of a drink of warm water containing a tablespoonful of sodium bicarbonate, which dissolves the mucus in the stomach ; this is returned, but leaves a clean and quiescent stomach. It must not be forgotten that a full rectum or bladder may much increase the tendency to vomit. In extreme cases gastric lavage should be resorted to, while Tr. Iodi, ♏i, or cocaine, gr. ss, by the mouth often will help.

Vomiting is far more liable to occur after a prolonged or unskilful anæsthetic, and in a nervous or frightened patient. Prolonged starvation before anæsthesia should be avoided as likely to cause acidosis and therefore aggravate any tendency to post-anæsthetic vomiting, which in these cases should be treated by drinks or infusion containing sodium bicarbonate and

5. Close the wound up carefully by one of the methods indicated in Chapter IV., p. 43, remembering that it is essential to approximate the deeper tissues in order to prevent hæmatomata and subsequent stretching of the scar.

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The patient should be encouraged to move about in bed and do as much for himself as possible from the time he recovers from the anæsthetic, as this, besides impressing the patient with his recovery, keeps his muscles in tone and may prevent complications, such as pulmonary embolus. Ordinary straightforward cases, such as herniæ in young people and quiescent appendices, should be allowed out of bed as soon as possible, usually when the clips or stitches have been removed, although as a general rule abdominal cases are kept in bed quite ten days; but patients after operations on the mouth, face, and breast are got out of bed within three days or so of operation.

Some surgeons prefer a more cautious convalescence, as they consider the patient recovers better from the nervous shock of the operation if kept in bed for a more prolonged period.

The diet of a patient after operation should be light, but consist of dry and solid food as well as liquids, large quantities of which

injection of doryl or pituitrin, 1 c.c. Hot bottles to the hypogastrium and to the feet will help. The administration of an enema also may have the desired result. If practicable, the patient may sit on the side of the bed or even stand up when micturition is usually prompt and easy, but if this is not permissible, catheterisation may have to be resorted to; this is, however, rarely the case.

Hysterical retention in women should not be treated by catheterisation, as such patients always will void urine when they are really uncomfortable. In this respect it always must be remembered that cases reported not to have passed water frequently have done so into the bed-pan when the bowels have been opened, in which case they are comfortable and the bladder not distended. In a few cases, especially after kidney, prostate or bladder operations, no urine may be passed as a result of "suppression," a condition which needs prompt handling in order to prevent uræmia. Hot enemata and copious drinks are usually efficient, but in severe cases more drastic measures may be necessary, such as hot packs, the administration of theobromine or sodium-thio-sulphate or sodium-thiocine-acetate.

(3) **Uræmia** may develop any time after operations on the urinary tract or in patients suffering from renal disease. Usually it is preceded by suppression, but sometimes large quantities of urine deficient in urea may be excreted. The blood-urea is high, the patient is usually drowsy or comatose, the skin dry, the tongue furred and the bowels costive; abdominal pain and distension are not uncommon, and twitching of muscles and convulsions usually herald a fatal result. The treatment is that of uræmia in general (see Vol. II., Chapter XX.).

(4) **Hæmorrhage** may occur during the first forty-eight hours after an operation from the slipping of a ligature, and is then known as "reactionary" (see p. 52): it must be promptly dealt with by taking the case back to the theatre, opening the wound and securing and ligaturing the bleeding point, after which morphia and, if necessary, saline may be given. Recognition is easy if the case is one of external hæmorrhage, though if "internal," as may occur after abdominal, pile or chest operations, the condition may be confused with "post-operative collapse"; but in hæmorrhage the pulse gets more rapid, restlessness and air-hunger develop, and the abdomen, if containing blood, becomes acutely tender on pressure, and may show shifting dulness.

(5) **Sleeplessness** may be troublesome, especially in nervous patients, and can often be cured by hot milk or whisky, but should this fail hypnotics, such as aspirin and bromide, nepenthe or medinal, may be necessary. A vast selection of good hypnotics is available.

(B) *Delayed Complications.*

(1) **Acute dilatation of the stomach** is a rare but usually fatal complication which may occur within the first few days after operation. The patient becomes acutely ill, collapsed, and vomits frequently and copiously; he frequently smells of acetone, and later becomes drowsy and dies in coma. Rarely jaundice may supervene. The stomach can be shown to be enormously dilated, it may contain over a gallon, and is atonic. Treatment consists in early recognition and gastric lavage. Placing the patient prone on his face is often useful (see Vol. II., Chapter XIV.).

(2) Another rare complication is **delayed chloroform poisoning**, a condition closely analogous to acute yellow atrophy of the liver, which is small and fatty, and on microscopy shows acute necrosis of its cells. The patient,

In cases where vomiting has caused acidosis and a vicious circle becomes established, as may occur in any persistent vomiting, relief can be obtained often by giving an injection of 10 units of insulin combined with barley sugar *ad lib.* to suck, while in more severe cases intravenous infusion of 20 units of insulin in ℥x of 50 per cent. glucose solution and ℥x normal saline is very efficacious

In neurotic subjects, who in many cases are determined before anæsthesia that they will be sick, every care must be taken to correct their mental outlook, and if vomiting persists absolute cessation of all oral feeding, not even allowing water to wash out the mouth, with administration of rectal salines four hourly, is always productive of a cure. Such treatment can be kept up for forty-eight hours and be repeated if necessary.

In any case of post-anæsthetic vomiting care must be taken not to alarm the patient and to re-establish confidence, while the practitioner must remember that a light dry diet is less likely to produce abdominal discomfort and vomiting than a long course of "slops." In cases where such diseases as peritonitis or uræmia are present, it must be realised that persistent vomiting after an operation is more likely to be due to these conditions than to the anæsthetic

POST-OPERATIVE COMPLICATIONS

These fall into two classes: (A) The Immediate; (B) The Remote.

(A) The *immediate complications* may occur during or within an hour or so after operation.

(1) **Cardiac failure and respiratory failure** may occur in the early stages of the induction of anæsthesia, when they are the result of sudden shock, or during or immediately following operation, usually as a sign of collapse, and call for prompt measures. Care should be taken that no foreign body, such as a denture, or vomited matter, is obstructing the patient's airway. These conditions, if due to anæsthesia, in which case their onset is sudden, fall to the lot of the anæsthetist to treat, and are dealt with in Vol. I., Chapter XXVI., but they may also come on gradually as the result of "*collapse*" induced by prolonged exposure or handling during an operation; the treatment in this case consists in finishing the operation as rapidly as possible, keeping the [illegible]

on the principle of "not flogging a tired horse" (Chapter IV., p. [illegible]). The [illegible]

miraculous effect as a resuscitant. For the same reason saline infusion should be avoided in these cases of post-operative collapse, for as the circulation is feeble the tissues easily become water-logged, and œdema of the lungs is a not uncommon and fatal result if infusions are given. Where, however, much [illegible]

of the condition, but, if possible, can be practised with advantage.

(2) **Retention of urine**, especially after pelvic operations, may be a difficult matter, but usually the patient will void urine following the oral administration of urotropin, grs. x, or Ac. Boric. ʒii in ℥i of water, or an

usually about ten days after operation, becomes delirious, and later comatose, vomits and shows signs of intense jaundice; death rapidly supervenes. These two conditions are now very rarely seen, probably more by reason of the abandonment of pre-operative starvation and purgation than from the lessened use of chloroform as an anæsthetic.

(3) **Uræmia** may be a late complication, but has been mentioned already.

(4) **Secondary hæmorrhage** may occur in septic wounds, usually about the tenth day after operation, and is often preceded by a slight initial hæmorrhage which occurs a few hours before the main bleeding. In cases where it is suspected, a close watch must be kept on the wound and pulse of the patient, and in cases of limb wounds a tourniquet kept over the bed. The condition will be dealt with fully in Chapter IV., p. 52.

(5) **Pulmonary embolism or thrombosis** (p. 268), the ætiology of which is unknown, is an increasingly common and very often fatal complication, which may occur any time from the fourth to the fourteenth day after operation, usually about the tenth day. It may follow the most trivial operation, but is commoner after operations on the upper abdomen, and seems to be predisposed to by the presence of sepsis in the wound, or by the co-existence of pulmonary complications, such as post-anæsthetic bronchitis or massive collapse. Patients kept very still in bed after operation appear to be more liable to the condition. Post-mortem, one or more branches of the pulmonary arteries, and maybe the main vessel and right ventricle, are found choked with clot, which may have formed as a result of ante- or post-mortem thrombosis; this clot spreads along the radicles of the pulmonary artery far into the lungs, but seldom yields any positive cultural result as regards bacteriology. Many pathologists regard the condition as one of thrombosis in the peripheral vessels of the pulmonary circulation, the clot spreading back to the great vessels and then suddenly increasing and impeding the heart's action. Certainly there is evidence that the older clot is usually at the periphery. The condition takes some time to develop after operation, and is less likely to occur if the patient moves about and breathes deeply. It is, however, difficult to explain the sudden onset of pain and dyspnœa on the hypothesis of a gradual thrombosis.

The signs are a sudden pain in the chest, with inability to breathe, the patient becoming first cyanosed and then ashy-grey and frequently dying at once. In some cases just before the onset the patient feels an intense desire to pass a stool; in less severe cases death may occur in a few minutes, but if the initial attack passes, the prognosis is good and recovery usually results, patients frequently thinking they have had a very severe attack of indigestion. Second, or even third, attacks may occur after a few hours' or days' interval, but these are most uncommon, usually less severe and rarely fatal. In these slighter attacks, hæmoptysis and the signs of consolidation with a dry pleurisy will be noticed. Thrombosis of deep veins, such as the femoral, not infrequently follows in a few days' time.

Treatment consists in the immediate injection of morphia gr. $\frac{1}{4}$–$\frac{1}{3}$ combined with atropine sulph. gr. $\frac{1}{100}$, and the administration of oxygen, and in reassuring the patient that the worst is over. Subsequently rest in bed for some days is necessary, as friction-rub and expectoration usually manifest themselves in the course of a day or so after the attack. (For Trendelenburg's operation see Vol. II., Chapter X.)

(6) **Massive pulmonary collapse** is an uncommon complication, and usually follows operations on the upper abdomen. The patient, usually th

operation, complains of discomfort and tightness in the chest and upper abdomen; an examination shows the lower part of the chest on the affected side to be moving badly, and auscultation reveals deficient air entry to the lower lobe. The temperature is sometimes high for a few days. An X-ray film shows the diaphragm to be raised and motionless. The condition may clear up in a day or two, or may be the precursor of other pulmonary affections or subphrenic abscess. Treatment consists in giving CO_2 inhalations, in applying a blister to the neck, to counter-irritate the phrenic nerve, and giving an expectorant mixture. Inhalations of CO_2 at the end of operation are a valuable prophylactic and may be repeated with advantage the day following operation in cases where pulmonary complications may occur (operations on the upper abdomen), and if such complications do occur.

(7) **Thrombosis of veins** *usually follows operations only when infection is* present in the wound. It may affect any vein, though the left femoral is most frequently affected, and the process is probably of the same nature as pulmonary "embolus." The affected part becomes swollen and tender, the vein may be seen or felt as a hard cord, and œdema can be demonstrated in the tissues distal to the affected part.

Treatment consists in keeping the patient in bed for at least three weeks, with the limb supported on pillows or in a cradle. After this time massage may be given gently for a week, and then the limb gradually brought into use. If the clots are infected they tend to disseminate and give rise to pyæmic abscesses, especially in joints and the lungs, a condition indicated by the appearance of painful inflammatory swellings or a friction rub with signs of broncho-pneumonia following on a rigor: in the case of abdominal wounds, hepatic abscesses develop from portal pyæmia; these may be many in number, in which case the patient becomes slightly jaundiced and the liver enlarged and tender, rigors are frequent; death supervenes rapidly in these cases of suppurative pylephlebitis (p. 293).

Chronic pyæmia may be a troublesome sequel in non-fatal cases.

(8) **Septicæmia** may supervene, especially where bone or joint operation wounds become infected.

These conditions are fully dealt with in Chapter V., p. 75, but it is perhaps well to draw attention to the necessity of opening and freely draining the infected wound.

(9) **Post-anæsthetic bronchitis and broncho-pneumonia** are dealt with in Chapter XXVI.

(10) **Delirium tremens** is a condition sometimes seen after operations, and also commonly in patients with fractures or other accidental injuries. It occurs in chronic alcoholics, usually as a result of deprivation of alcohol, and manifests itself three or four days after admission. The patient is usually morose and suspicious, and towards night becomes very wakeful and prone to hallucinations, to see "things," or hear persons conversing. If untreated, these get worse and the patient will rise from bed to remove imaginary objects, or to escape from animals or enemies; during the day there is mental

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bowels moving freely. Once the condition has developed alcohol should be given, and strong purgatives administered to open the bowels, which are usually very obstinately costive in spite of treatment. The patient needs reassuring, and gently and tactfully restraining from leaving the bed—violent

restraint only aggravates him; sedatives, of which the best is Inj. Hyoscine, gr. $\frac{1}{100}$, combined with morphia, gr. $\frac{1}{4}$, should be given. Large doses of chloral and bromide are useful.

(11) **Post-operative mania** is a rare but frequently fatal complication usually seen in pregnant or neurotic women and following operations on the pelvic organs; rarely however it may occur in men, and Jews seem particularly liable to it. The patient develops acute mania, usually with suicidal tendencies, and needs immediate isolation and constant watching and care, if possible in a mental institution

(12) **Post-operative hiccough** is an irritating phenomenon seen sometimes after abdominal operations, when it may persist for several days. In some instances it is of serious import implying the onset of uræmia or peritonitis, in which case other signs of these conditions will be present including a dry tongue More often it is a distressing phenomenon and ceases during sleep, in which case it is best treated by reassuring the patient, and giving small doses of cocaine or morphia, while in some cases a change of position is beneficial.

CHAPTER II

INFLAMMATION

Its Relation to all Tissue Repair—Acute and Chronic Inflammation—Clinical Signs—Abnormal Repair—Scars

Inflammation may be best defined as the normal reaction of the body tissues to any irritant, be that in the form of trauma, infection or new growth. This irritation may be the result of injury, of surgical operations, of bacterial infection, or of new formations of abnormal tissue. The resulting inflammatory process called forth in the affected area is, in its initial stages, the same in every case; in the later stages local conditions, both as regards the reaction of the tissue affected and the cause calling forth this initial inflammatory reaction, may much modify or even mask the results of this common early stage.

The causes of irritation may be classified into:—

1. Mechanical. Blows, wounds, fractures, strains, etc.
2. Thermal. Burns and scalds, frost-bite.
3. Electrical. Lightning stroke, X-ray burns.
4. Chemical. The action of caustics, strong acids, etc.
5. Bacterial. Various micro-organisms.
6. Neoplasms (new growths) which cause intense reaction in the surrounding tissues.

These will be considered in detail later, as both in their physical signs and ultimate inflammatory results they differ widely in their effect on the organism; here, where only the initial stages of the common inflammatory reaction produced by all these cases are under consideration, it will be unnecessary to differentiate them. It is, however, necessary to say how very

of function. Clinically, it is often difficult to separate the immediate signs of injury to the tissues, such as the mechanical effusion of free blood from damage to vessels in the affected area, from the early stage of the inflammatory reaction, with its passive transudation of fluid through the vessel walls.

Both these conditions give rise to a certain amount of swelling in the region, which may be very considerable in areas where the connective tissue stroma is lax, *i.e.*, the scrotum and eyelids. Inasmuch as this swelling is due to fluid lying free among the tissue cells, the area is found to be boggy to the touch and to retain the impress of the examining finger, *i.e.*, to pit on pressure, signs denoting a condition of *œdema*.

The inflamed area in addition will be found to look red, as compared with the surrounding parts, and to feel hot, both conditions being due to the increased blood supply consequent on the inflammatory reaction.

Owing to pressure of fluid on nerve endings the area is painful and tender, and for this reason, from the effect of the exudation on muscles and nerves,

the movement of the part will increase this pain, and the affected region is kept still by the patient—*i.e.*, there is loss of function.

Pathology. Turning to the micro-pathology of this condition, a subject best studied by examining the behaviour of the tissues of a translucent area, such as the web of a frog's foot, to which an irritant has been applied, it will be found that the sequence of events observed is the same whatever irritant is employed—that is to say, the inflammatory reaction of the tissues is the same to a cut as to a bacterial infection. The first change observed is a *dilation of the blood vessels in the tissues* around the source of irritation, with an *acceleration of the blood stream.* This increased rate of blood flow is, however, only very transitory, and is succeeded by a gradually *increasing slowing of the blood stream,* which may proceed to actual stoppage, with subsequent thrombosis of the vessel

At the same time a change can be observed in the blood; the red corpuscles, as a result of the slowing of the blood stream, tend to accumulate in rouleaux in the centres of the vessels, while the white corpuscles adhere to the endothelium, and later can be seen passing through the vessel wall in large numbers (*diapedesis*) and lying among the surrounding tissue cells. This change is most marked in the immediate vicinity of the irritant, and is much more obvious in cases of bacterial infection than in other cases.

The exact mechanism by which this exudation of leucocytes occurs is not known, but it probably takes place between the endothelial cells as a result of disintegration of the cement substance—certainly red cells and plasma escape also, showing there is leakage through the vessel wall. As soon as thrombosis occurs, exudation from that area ceases.

It is of great interest to note that in acute inflammatory conditions the common type of white cell is the polymorphonuclear leucocyte, which is exuded in numbers far in excess of that found in the blood stream, whereas in chronic inflammation the predominant white cell is the small lymphocyte.

Turning now to the changes in the tissues around, it can be seen that there is an accumulation of fluid between the cells; this is derived mainly from the vessels, and may in some cases, as in the blisters from burns, be so excessive as to separate the cells and disintegrate the tissues, a condition known as *colliquative necrosis.* This fluid can be shown to be rich in various antibodies (p 35), and plays an important part in tissue repair.

The red cells after transudation are rapidly broken up and their pigment reabsorbed, though it frequently causes discoloration in the area during the process.

The white cells may return to the vessels, but more frequently actively migrate, by diapedesis, towards the source of irritation, being apparently actively attracted to this region (positive chemiotaxis), though in some few cases they will be found to be repelled from the irritant (negative chemiotaxis). The white cells and plasma are to be regarded, therefore, as the tissues' first line of defence. They are accumulated in great numbers around the irritant, which, under favourable circumstances, they eliminate before proceeding to restore the surrounding tissues to their normal conditions—a process known as *Resolution.*

Resolution and Repair are the most favourable results of inflammation, and usually follow after non-bacterial irritation; they are accompanied, both clinically and microscopically, by retrograde changes, with gradual return to normal conditions. Thus, clinically, the pain, tenderness and redness get less, the œdema and swelling disappear, and the affected tissue resumes its normal

function, though in the case of special tissues such as bone and nerve (peripheral) it may be a considerable time before full restoration of normal tissue is complete, *if indeed this ever occurs; in the case of the brain and* spinal cord regeneration never occurs. Microscopically, the cells return to the vessels, the blood stream accelerates (actual thrombosis is not likely to have occurred), the plasma is absorbed and the part returns to normal. In cases where this process has taken a considerable time (chronic inflammation), there are certain permanent changes *in the tissue, due to the formation of* cells known as fibroblasts in and around the exudation. From these cells fibrous tissue is developed, which to a varying extent strangulates the vessels and *cells of the part*, with the result that it becomes distorted and more or less avascular, a condition clinically manifested by *scarring* of the tissues and thickening around the inflamed area due to formation of new tissue elements (*organisation*).

Frequently the later stages of the inflammatory process do not result in so *favourable an ending as described, this depending on various factors* such as the nature of the irritant applied, a bacterial infection being much less favourable to resolution than any other cause. Again, such factors as the virulence of the infection and the local resistance of the tissues must be taken into account, as is shown by the fact that different cultures of the *same organism may produce different degrees of inflammation if injected* into the same tissue, or that the same tissue in different individuals will give very different reactions if injected with the same culture in equal amounts.

These less favourable results of the inflammatory reaction, indicating as they do that the tissue cannot cope with the irritation produced by the *poisons resulting from the bacterial infection, which is usually the fons et origo mali* in such cases, are marked by a common stage, transitional between the early stages of normal tissue reaction just described, and the later stages where the inflammatory processes are masked and modified by the local conditions.

Clinically the earliest sign of serious trouble is that the increased redness in the area does not disappear on pressure ; this can be shown to coincide with the vascular thrombosis, which naturally prevents the blood being expressed

infection. The tissues now call up reinforcements in an attempt to localise the infection, with the result that there is an increase in the area affected by the inflammatory process—to what extent is determined by the success or otherwise of the *attempt at localisation* ; the *greater the success the less will*

are due mainly to the absorption of toxins from the inflamed area, and will be the more marked the greater the tension of the *inflammatory products* in the area affected ; thus a small bead of pus under great tension, *i.e.*, in the tissues lining the external auditory meatus, will produce far greater constitutional signs than a large abscess in the loose cellular tissue beneath the pectoral muscles or in the scrotum, because of the toxins being more readily absorbed when under pressure.

The constitutional signs are *fever* which is usually of the intermittent type,

the temperature being at its highest about 8 p.m., and lowest, usually normal, about 8 a.m. daily; this is accompanied by a more or less *rapid heart beat, dry tongue and mouth, headache, general malaise* and *scanty high-coloured urine. Shivering* and *vomiting* may occur at the onset of the disease. There is frequently loss of appetite, and in long-standing cases muscular wasting, weakness and constipation.

It should be noted that occasionally in cases proceeding to resolution, [illegible] has been considerable effusion of blood into the tissues, *i.e.*, after fractures and in wounds after operations, especially where a *hæmatoma* has occurred.

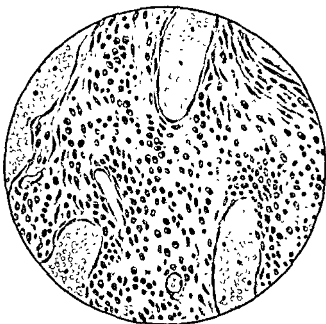


FIG 4 Granulation Tissue from a peritoneal adhesion, showing plasma cells and fibroblasts. × 200.

It is by some regarded as due to the absorption of fibrin ferment from the clot, and by others as resulting from mild infection with the *Staphylococcus albus,* usually to be found in all such clots.

According to the success or failure of the tissues in localising the infection, one of the following results will occur:—

1. Abscess formation.
2. Cellulitis
3. Local gangrene (death of tissue).
4. General infection of the body—septicæmia, pyæmia, sapræmia.

All of these conditions are dealt with in the chapter on *Infection,* as they are to be regarded rather as the sequelæ of infection than as an integral part of inflammation.

Regeneration. Normally, resolution of the inflammatory process is succeeded by a process of tissue repair (*regeneration*), the tissues of the part, if damaged by the irritant, being gradually restored to their normal structure; thus, after a fracture the bone becomes differentiated from [illegible]

and reformed, a process which takes longer than the repair of the surrounding soft parts.

New capillary vessels are formed among the exudate, budding out from the sides of existing capillaries, and joining with other buds to form loops, around which appear fibroblasts and plasma cells. Thus there is formed a very vascular mass of soft, friable tissue, bright red in colour and bleeding easily to the touch; it is known as *granulation tissue*, and is well seen on the floor of a clean healing ulcer. In the case of an incised wound with the edges approximated, it is very small in amount, as the surrounding tissues are in contact and soon re-establish their continuity, a condition known as **healing per primam**; whereas in ulcers and lacerated wounds where much tissue is missing and a space exists filled with blood clot the replacement of this clot by granulations is a slower process (**healing by granulation**), which can sometimes be accelerated by approximating two granulating surfaces (**healing by union of granulations**), a process only to be attempted in the absence of infection of these granulating surfaces.

The *fibroblasts* are elongated cells, which throw out a series of fibrils in and around their cytoplasm which gradually elongate and narrow down the original cell, and by their contracture give firmness to the new tissue, ultimately becoming so numerous as to result in constriction of the vessels and obvious scarring in the area.

The *plasma cells*, which are irregular in shape and contain granules in the cytoplasm, are distributed among the capillaries and form a stroma, from which the tissue cells may regenerate; or perhaps they act merely as a scaffolding along which the cells of individual tissues grow out into the injured area and ultimately reform it.

This repair is brought about by changes in the scar and granulation tissue in the area, which it will be remembered consists of blood vessels, plasma cells and fibroblasts, but the regeneration of tissue is usually more or less imperfect, so that some fibrosis and scarring persists in the affected area. Usually the longer the irritation has persisted, the greater the resulting scarring; hence extensive fibrosis is more common in cases where infection has been present, or large areas of tissue have been affected or lost by sloughing

The treatment of inflammation is more aptly dealt with under the various types of inflammatory reactions called forth by different irritants in the body, but it may not be out of place briefly to enumerate here the essentials of the treatment necessary in any inflammatory reaction:—

1. *Removal of the cause of irritation* whenever practicable, or the reduction of the irritant to a minimum if its total removal is not possible. To attain this end the area may be excised or treated with the cautery or caustic; but as this in many cases entails severe damage to tissue, it is frequently advisable to content oneself with less drastic measures which aim at the removal of as much irritant as possible while not damaging the tissues more than is necessary or compatible with their subsequent utility. Such methods consist in incisions, drainage, and means to promote freer blood and lymph supply which serve to remove the source of irritation from the locality and are fully described in Chapter III., p. 27.

2. *Rest and support* to the inflamed area, in order to lessen pain and to localise infection.

3. *Promotion of increased blood and lymph supply* to the area, so as to bring reinforcements of, white cells and antibodies to deal with the source of irritation. This also serves to dilute and carry away the irritant, but unless

A SYSTEM OF SURGERY

SURGICAL BACTERIOLOGY

BY GEORGES DREYER, C.B.E., M.A., M.D., F.R.S.
AND
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I. INTRODUCTORY

The importance of bacteriology for modern surgery cannot easily be overestimated. For, besides its obvious and now well-recognized relation to surgical cleanliness in the management of wounds, it often proves itself of the utmost value in prognosis, it not infrequently affords very great assistance in the treatment of infective processes, and it is essential in establishing a certain diagnosis in many otherwise doubtful cases.

The surgeon cannot be too careful to take every advantage which bacteriology affords of acquainting himself with the precise character of every infection he is called upon to treat, and the actual identity of its causal agents; nor can he be too well informed as to the nature and the mode of action of the micro-organisms with which the tissues of his patient have to deal.

The methods of bacteriology are in general extremely simple, and all the information required can in very many cases be both easily and quickly obtained. A microscope, some slides, one or two stains, and a few culture-tubes should be as much a part of the surgeon's arsenal as a catheter or a scalpel. Even where the opinion of an expert bacteriologist is found to be desirable, a microscope-preparation and a culture which were made at once on opening an abscess, for example, will not infrequently enable him to give much more certain and reliable information to the surgeon than is likely to be obtained by any examination of the same material after the lapse of perhaps hours, or, it may be, a whole day. In bacteriological material which has not been dealt with at once, the death and disappearance of more

delicate micro-organisms, and the rapid multiplication of the more robust types, will often completely alter the bacteriological picture. The examination may then entirely fail to reveal the true nature of the infection, or even give a purely negative result. Moreover, at a time when treatment founded on bacteriological methods is being widely extended, and the use of vaccines as protective and curative agents is being more and more generally attempted, it is of the utmost importance that the surgeon should make himself familiar with the principles which underlie this method of treatment, so that due regard may be paid to the need for accurate bacteriological diagnosis. Equally essential is it that wide clinical knowledge and experience should invariably direct and control its application.

Although the idea that unknown minute forms of life might be the causal agents of disease was suggested even in the pre-Christian era, and again brought into prominence by writers of the seventeenth, eighteenth, and early part of the nineteenth centuries, the history of pathological bacteriology begins for all practical purposes with Pasteur. His epoch-making studies, between 1850 and 1860, of the phenomena of putrefaction and fermentation, which gave the death-blow to the theory of spontaneous generation, at the same time proved beyond question that those processes were due to the intrusion of active extraneous living micro-organisms. The discoveries of Pasteur arrested the attention of the civilized world, and his results were soon confirmed by numerous observers—in this country more especially by Tyndall, Burdon-Sanderson, and Lister. The practical genius of Lister speedily realized the vast importance which these discoveries possessed for operative surgery, and, in particular, for the events associated with the healing of wounds, and grasped the immense advantages which would result from the discovery of means for getting rid of harmful microbes from the field of surgical operations. Following the path marked out by the investigations just referred to, his own laborious studies (1867) laid a sure foundation on which, unaided, he was able to raise the noble edifice of antiseptic surgery, and thereby confer inestimable benefits upon mankind at large. His claim to gratitude is not diminished by the fact that fuller knowledge has developed antiseptic methods into aseptic ones, for antisepsis, and antisepsis alone, made the aseptic treatment possible.

While Lister was engaged in proving the necessity, and providing means, of getting rid of micro-organisms in general in operative surgery, other observers were following out the illuminating work of Pasteur along other lines, and presently succeeded in establishing bacterial specificity in a number of diseases. Davaine, who, in 1850, had already observed the presence of rod-like micro-organisms in the blood of animals that had died of anthrax, without definitely

associating them with the causation of the disease, now returned to the subject (1863), and showed that such blood was only capable of transmitting the disease to healthy animals when these rods were present in it. He was confirmed, in 1876, by Robert Koch, who succeeded in obtaining pure cultures of the organism, and by his experimental observations clearly proved the specificity of the bacterium in question.

In 1881, Koch made his first great contribution to bacteriological technique by the introduction of the use of gelatin as a culture medium. This discovery inaugurated a new era in the investigation of bacterial infections, by enabling pure cultures of bacteria to be prepared with ease and certainty. In the same year Koch was led in the course of his exact investigations to advance those postulates for bacterial specificity in disease which are still accepted as fundamental principles. His observations soon attracted universal attention, and from this period dates the rapid development of modern bacteriological research. The simplification of the culture methods, and the introduction about the same time, by Ehrlich, Weigert, and Koch, of aniline dyes as stains for micro-organisms, smoothed the path for the army of patient and acute investigators who now began to work upon the problems of infection.

The extraordinary activity of the last forty years in this most fertile field of scientific study has resulted in an advance unequalled in rapidity and in importance in the whole history of pathological investigation, and has led to those discoveries regarding the etiology, the progress, prophylaxis, and specific treatment of a large number of infections which have entirely revolutionized the aspect of modern medicine.

II. GENERAL BACTERIOLOGY

A. GENERAL MORPHOLOGY AND DEVELOPMENT

1. FORM AND SIZE

Bacteria are minute vegetable organisms which possess a uniform and usually well-marked outline, and, though varying considerably in shape, may be broadly classed under the headings spherical or rounded (cocci), rod-shaped (bacilli), curved rods (vibriones), wavy elements (spirilla), screw-shaped organisms (spirochæta), and filamentous forms (streptothrix, etc.). On the average, the diameter of a coccus varies between 0 5–1 μ ($\mu = \frac{1}{1000}$ mm.), while the rods, whether straight or curved, may possess a length of from 1–6 μ, or even 8 μ or more, with a diameter of from 0 2–0 6 μ in different cases. Thus, *Bacillus*

anthracis has a length of 3–10 μ, with a breadth of 1–1·5 μ, while *B. coli* only measures 2–4 μ by about 0·5 μ wide, and *B. influenzæ* is still smaller, being less in length than the width of *B. anthracis* and measuring about 0·5–1 μ long, by 0·2–0·3 μ wide.

Between the groups already mentioned occur intermediate forms, which it may be difficult to assign to the one class or the other. Hence has arisen the use of such terms as coccobacillus (e.g. *B. prodigiosus*) and the like. Moreover, in each group itself considerable diversity of form appears. Thus, among the cocci we may note well-rounded forms like staphylococci, bean-shaped or kidney-shaped bodies like the gonococcus and meningococcus, and lanceolate organisms such as the pneumococcus. Among the rods still greater diversity is found. They may be quite straight in outline as is the *B. tetani*, or be slightly bent as is the bacillus of tuberculosis; they may have sharply cut ends like *B. anthracis*, or be rounded off like the *B. subtilis*; and they may be irregular, swollen at the ends, or even club-shaped, as, for example, is frequently the case with the *B. diphtheriæ* and the diphtheroids.

2. ARRANGEMENT IN SPACE

The arrangement of bacteria in space depends largely on their mode of growth and manner of multiplying by the division of one organism into two new independent individuals (*see* p. 7), and on the degree of adhesion which remains between the new individuals thus formed. Among the cocci, division may occur in one direction only, in two directions mutually at right angles, in three directions at right angles to each other, or in an indefinite number of directions, and more or less adhesion may persist between the new elements, thus giving rise to single elements, diplococci, streptococci, tetrageni, sarcinæ, staphylococci, and the like. Similarly, among the rods, where division only occurs in a direction at right angles to the long axis, varying degrees of adhesion among the individual bacteria give rise to an arrangement as either separate organisms, paired forms, or not infrequently chains. Among the curved rods very similar appearances are found. The filamentous forms may present, in addition to the ordinary method of division or in place of it, the phenomenon of "branching" or bifurcation, but into this it is not necessary to enter here.

3. CLASSIFICATION

An adequate classification of bacteria, on the basis of morphology, physiology, or life history, is at present impossible; it must suffice therefore to group them under headings indicative of their form and arrangement, which shall serve for their convenient identification. Such a provisional classification, based on that of Cohn, is given

below. Nevertheless, it must be clearly understood that the description "single organisms," "pairs," "chains," and so on, cannot be strictly applied, but refers only to the *general appearance* presented by a microscopic film. Thus, among diplococci, for example, many single organisms will be found, among the staphylococci numerous single individuals and perhaps many pairs, and similarly in other instances.

PROVISIONAL CLASSIFICATION OF BACTERIA

ROUNDED ORGANISMS (COCCI)	*Monococcus:* Single organisms separating after division.
	Diplococcus: Remaining in pairs after division.
	Tetragenus: Dividing in two directions at right angles to each other, thus giving rise to an arrangement in fours.
	Sarcina: Dividing in three directions mutually at right angles, thus giving rise to packets of eight.
	Streptococcus: Dividing in one direction only, the new organisms remaining in contact to form "chains."
	Staphylococcus: Dividing in all directions, the organisms are massed together in irregular clusters.
	Ascococcus: Dividing like the staphylococcus, the clusters produced are enclosed within a membrane and form a nodulated mass.
STRAIGHT RODS (BACILLI)	*Monobacillus:* Single organisms, separating after division.
	Diplobacillus: Remaining in pairs after division.
	Streptobacillus. Remaining connected and forming chains or threads
CURVED RODS	*Vibrio:* Curved single or paired organisms.
	Spirillum: Remaining connected after division and forming wavy threads.
	Spirochæte: Single uniform screw-like threads, more sharply bent than the spirilla.

Of the higher bacteria, or filamentous forms, the only group at present of surgical interest is that of the Streptothriciæ, in which the filaments often exhibit branching. To this group belong the ray fungus (the actinomyces) and the *Streptothrix maduræ*.

4. STRUCTURE AND CONSTITUTION

The bacteria are highly refractile, sharply-contoured, colourless or more or less pigmented masses of protoplasm, which may be regarded as individual cells, but which exhibit staining properties more akin to those of nuclei than of cell protoplasm in general.

The closer study of their intimate structure has been pursued in the main by three chief methods, viz. the artificial production of plasmolysis, staining with aniline dyes, and chemical or microchemical analysis.

Plasmolysis is produced by placing the cells in question in salt solutions of higher concentration than that normal to the cells themselves, thus withdrawing water. This causes the cell protoplasm to shrink away from the envelope of the cell, leaving a space between.

The bacterial cell consists of (i) an envelope, (ii) a cell protoplasm containing vacuoles and granules, and exhibiting in certain instances what some observers have regarded as a nucleus; and in many cases (iii) *flagella* projecting outwards from the envelope. The cell body may also contain a greater or less amount of (iv) pigment.

i. **Envelope.**—The envelope is a thin membrane, the presence of which can be well shown by the method of plasmolysis. Its outer limits are usually *ill* defined, probably owing to a tendency to take up fluid from the surrounding medium and become swollen out, thus giving it the appearance of a halo. Such a halo when sufficiently well marked is termed a *capsule*. The presence or absence of a definite capsule is accordingly found to depend to a great extent upon the conditions under which the particular organism has grown.

The chemical constitution of the envelope is albuminous in character, but in some cases varying amounts of carbohydrate (e.g. cellulose) are said to be present, as for example in the common sarcina of the stomach (*Sarcina ventriculi*) or the *Clostridium butyricum* found on potato skins.

ii. **Protoplasm.**—The protoplasm is a semi-fluid material yielding on examination proteins, salts, and water, as well as various metabolic substances. In appearance it is homogeneous or finely granular, newly-formed cells being usually homogeneous, but becoming granular and often vacuolated as they develop. In old cells almost the whole of the interior may be occupied by several vacuoles, or more frequently by a single large one. The "granules," which may vary in number from only one or two to half a dozen, show a great avidity for certain aniline dyes, and have in consequence been spoken of as "chromatin" granules. One or more of them has sometimes been supposed to represent a nucleus, but that this is actually the case is very improbable, since they have never been observed to divide during the division of the bacterial cell. Other well-defined, strongly refractile granules are to be found in particular groups of bacteria, and have been shown to consist of sulphur in a free condition.

The bacterial proteins appear to contain on analysis rather less nitrogen than animal proteins (about 1 per cent. less), and have accordingly been grouped together under a special heading as *mycoproteins*. They are in many respects akin to the nucleins, but differ from them in that in some cases, at any rate, phosphorus has not been shown to be a necessary constituent.

iii. **Flagella.**—By far the greater number of motile bacteria are provided with one or more flagella. These are whip-like processes

projecting from the bacterial envelope, but almost certainly arising from the cell-protoplasm within. They can best be demonstrated by special staining methods, though they can also be seen by using reflected light on a dark background. They may be terminal (polar), and may then be single, as usually in the comma bacillus (*Vibrio choleræ asiaticæ*), or several in number, forming a brush at one end, as in the *B. cyanogenes* of blue milk; or they may be distributed all round the organism (peritrichate), and may be numerous, long and wavy as in the case of *B. typhosus*, or comparatively few and short as in *B. coli.*

iv. **Pigment.**—Many bacterial cultures are highly pigmented, and different varieties exhibit red, orange, yellow, green, blue, or violet coloration. The pigment, though in some cases it is found within the bodies of the bacteria, is usually present as an excrete product between the bacterial cells, or diffused out into the surrounding medium. The subject is more fully dealt with under the heading of Metabolic Products (p. 18).

5. REPRODUCTION

The bacterial cell propagates itself by direct division into two new individuals, and in some cases also it maintains itself by the method of spore-formation.

i. **Direct division.**—Among the rods, increase in length occurs until the organism has grown to nearly double its original size, the transverse measurement meanwhile remaining unchanged. Fission then takes place by the appearance of a dividing membrane which arises from the envelope around the middle of the rod, and grows inwards to complete a transverse septum, thus converting the single organism into two new ones. The septum splits across, and the new individuals become independent entities. After the division is complete the young organisms, which may not yet have reached their full development, continue their growth. In this way multiplication proceeds rapidly, and the new organisms may separate to a greater or less extent in accordance with the particular habit of the type concerned. (*See* p. 4.)

In the cocci the events are somewhat different. There is usually either no growth, or only a slight increase in all diameters, before the dividing membrane appears which separates the single organism into two. The division is followed by increase in size, and by a restoration of the typical form of the organism concerned.

The rate of reproduction of the bacteria varies within wide limits, and is dependent both on the particular variety concerned and on the conditions under which it is placed. In favourable circumstances multiplication is extremely rapid, and may take place as often as once

in every twenty or thirty minutes. If this rate were kept up continuously a single organism would give rise to a colony of about 30,000,000,000,000 (thirty billions) in the course of 48 hours. But such rapid growth only occurs when all the conditions are peculiarly favourable, and in cultures grown under ordinary limitations the rate of multiplying speedily decreases as the organisms become numerous and crowded. Moreover, it is found after a comparatively short period that in such culture a considerable number of the organisms are already dead. Different organisms and different kinds of culture exhibit wide variations in this respect.

ii **Spore-formation.**—A number of bacteria possess the faculty of producing "spores" These tend to appear when the conditions become less favourable to vegetative growth. They are specially resistant *resting forms of the organisms concerned, and are produced* within the vegetative cell. A tiny bead-like granule appears which, as it grows, takes in a greater or less amount of the bacterial protoplasm and becomes surrounded by an extremely dense membrane. Or several granules may appear and ultimately fuse to form the spore, which thus presents itself as a thick-walled, highly refractile body, without vacuoles, and containing very little water in its protoplasm. Accordingly it exhibits a remarkable resistance to unfavourable *conditions.*

The spores thus formed may be spherical or egg-shaped, and may be situated either centrally or towards one end of the bacterial cell, whose outline may or may not be altered by their presence. In the case of *B. anthracis*, for example, the rod is unaltered in shape; in other cases a variety of different forms are produced to which such terms as spindle-shaped (*clostridium*), *cuneate*, *clavate*, and *capitate* have been applied.

In the case of most bacteria only a single spore is formed by the vegetative cell. The cell usually then breaks up, and the spore is set free. When the conditions of life again become favourable, germination of the spore takes place either by polar or equatorial dehiscence of the spore-membrane. The process is initiated by a general swelling of the spore, which takes up water, and becomes less obviously refractile, assuming more the appearance of a vegetative cell, and a new bacillus grows out from its protoplasm at the point of rupture of the enveloping membrane.

Spores are *not* to be regarded as a normal stage in the multiplication of the bacteria concerned, but only as a special method of defence against injurious influences. Thus, while *B. anthracis* is killed by exposure to a temperature of 70° C. for about five minutes, its spores require boiling for about an equal time to ensure their death. Again, *B. subtilis* is killed by five to ten minutes' heating at 70° C., while at least

an hour's boiling is necessary to destroy its spores. Bacterial spores are indeed the most resistant forms of life with which we are acquainted, and a number of the pathogenetic micro-organisms belong to the group of the spore-forming bacteria (e.g. *B. anthracis*, *B. tetani*, *B. œdematis maligni*, *B. welchii*). Spore-formation is only known with certainty among the bacilli, and it is still a question whether it is ever found among the vibriones and spirilla. Cocci do not form spores, though formerly it was supposed that certain larger, deeply staining individuals sometimes seen among the other members of a chain of streptococci, for example, possessed resistant properties akin to those of spores. Accordingly they were given the name of *arthrospores*. It is now clearly proved, however, that these so-called arthrospores possess no greater resistance than the other individuals in the same culture, and are, therefore, not spores at all.

6. MORPHOLOGICAL VARIATIONS

Morphological variation is extremely common among bacteria. So much is this the case that certain organisms have been said to exhibit pleomorphism. In addition to this a very large number show so-called involution-forms whenever the conditions of life become at all less favourable than the optimum as regards food, temperature, etc.

True pleomorphism, however, cannot properly be said to exist unless it is shown that the particular organism in question can exhibit more than one morphological type when growing under the most favourable conditions. This has not yet been adequately demonstrated in a single instance. But the fact appears to be that the precise form, size, arrangement, provision of flagella, and the like in particular bacteria are highly variable characters, and that almost any and every important change in environment may lead to more or less considerable changes in the morphology of the bacterium concerned. Such changes do not constitute permanent modifications of the bacterial type, but are mere fluctuations within the limits of variability of the species. Examples of divergences of similar degree are often found within the population of a single culture.

7. NAKED-EYE APPEARANCES OF GROWTH

When bacteria have been isolated in pure culture, and are grown in different artificial media, they frequently present more or less characteristic and distinctive appearances. These are often of the greatest value for diagnostic purposes, since naked-eye inspection alone may afford an important clue to the identity of the bacterium concerned.

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Moreover, the general features of a bacterial growth are largely dependent on the nature of the medium employed, and particularly on whether it is fluid or solid in character. It is therefore desirable here to indicate in general terms the points of special importance for the differentiation of bacterial cultures by the naked eye.

In a **fluid culture medium** a bacterial growth may distinguish itself by the presence or absence of a pellicle growing on the surface. This, if present, may be thick and copious, or scanty; it may be smooth, or wrinkled, in appearance; and it may be pigmented, iridescent, or colourless. In other cases there may be a froth upon the surface of the fluid as the result of gas production by the bacteria. The fluid itself is either rendered turbid by the micro-organisms distributed throughout it; or it remains clear, the growth appearing in the form of larger or smaller flocculi or granular masses, which may remain suspended for a longer or shorter period, or fall as a deposit to the foot of the tube. Such a deposit may be more or less copious; it may be cotton-wool-like in appearance, or flocculent, or stringy when shaken up, or dense and heavy; and it may be either pigmented or colourless.

When the bacteria are grown on **solid media** the appearances depend to a great extent on where the development takes place, whether upon the surface of the medium or in the substance of it; and upon whether the bacterial growth is fused together, presenting a continuous mass, or appears in the form of separate colonies.

A fused growth upon **a surface** may be thick and copious, or thin and scanty; it may be smooth, or granular, or even wrinkled; of a dry or moist appearance; and colourless, or fluorescent, or pigmented. The surface of certain media (e.g. gelatin) may be variously pitted or excavated by liquefaction.

In **the depth** the points of special interest are the occurrence of gas-formation and of pigmentation. In addition to these, where a stab culture is concerned, the manner of the growth is of importance Thus it may result in liquefaction (e.g. in gelatin media or coagulated serum), it may exhibit lateral offshoots from the vertical stem—the so-called "spiking"—and it may be most luxuriant in the lower part of the stab, or near the surface, according as the presence of oxygen is or is not inimical to the organism concerned.

When the growth is represented by **separate colonies,** additional information may be gained from an observation of their form and size, and of their outline, structure, density, and colour. In many cases the appearance of the surface colonies in pure cultures is by no means uniform, and the surface colonies also differ considerably in shape, size, and outline from the appearance presented by colonies in the depth of the medium.

B. GENERAL BIOLOGY OF BACTERIA

1. CONDITIONS OF LIFE

The conditions of life which affect bacteria may be considered first in respect of their absolute requirements or essential needs, and secondly in relation to the general effects produced by the particular character of their environment, and by variations in that environment.

i. **Essential needs.**—For all bacteria a suitable supply of food, moisture, and inorganic salts is necessary to vegetative growth. In many cases also either the presence or the absence of oxygen may be absolutely essential, though in many others it is a matter of greater or less indifference. Temperature is of great importance to bacterial life, each variety exhibiting its optimum of growth between comparatively narrow limits of temperature, though the range of possible growth may extend over a considerable number of degrees.

All bacteria require carbon, hydrogen, nitrogen, oxygen, and water, as well as salts, among which those of calcium and potassium are specially important. Some of them are able to obtain these substances from quite simple sources, while others can only take them from more complex compounds, and others again appear to find a suitable environment only within the body of a living animal. Accordingly they have been divided into such groups as "obligatory parasites," living only in the body of a living animal; "facultative saprophytes," living by preference in the living body, but capable of an external existence; "facultative parasites," which normally exist as saprophytes, but can continue to live within the tissues of an animal; and "obligatory saprophytes," which cannot grow at all within the living animal body.

A classification of this kind is important in its pathological aspects; but the separation of a particular class of micro-organisms as necessarily parasitic in the living body must not be taken to imply more than that suitable conditions do not, so far as we know, exist elsewhere in nature It may be, and in certain cases is already, possible to provide them in the laboratory.

An artificial medium for bacterial culture must contain in a suitable form the essential elements already mentioned, and must preferably possess a slightly alkaline reaction. In this respect the bacteria differ from the fungi and higher plants which require for their growth a slightly acid or neutral reaction in the soil in which they grow. Some bacteria, however, can grow in acid media, and may even themselves produce various acids in considerable quantities; while others again refuse to grow at all unless an acid medium is supplied to them.

A number of bacteria, among which are included some of the most important pathogenetic forms, require for their most favourable

cultivation, in addition to the essential materials already mentioned, special substances of complex constitution, such as hæmoglobin. But the details of these peculiarities will be dealt with more conveniently when we discuss the particular micro-organisms in question.

ii. **Effect of environment.**—While bacteria in general possess a remarkable power of adapting themselves to their surroundings, yet on the other hand *they exhibit in some cases an almost* equally remarkable susceptibility to quite small changes in particular features of their environment. A number of these are of sufficient importance to require individual discussion.

(*a*) **Relation to free oxygen.**—Until the discovery by Pasteur, in 1861, of "anaerobic" micro-organisms, the presence of free oxygen had been regarded as essential to the continued maintenance of every form of life. The investigation of bacterial forms to which free oxygen is actually harmful threw a new light on the physiology of these organisms, and led indirectly to a fresh advance in the study of bacterial disease. It is now known that while to some bacteria a supply of free oxygen is absolutely essential (obligatory aerobes, e.g. *B. subtilis* and *B. aceti*), to others its entire absence is equally necessary (obligatory anaerobes, e.g. *B. tetani* and *B. œdematis maligni*) But to the large majority the oxygen supply is to a greater or less extent a matter of indifference, since in the absence of *free* oxygen they obtain what they require from the decomposition products of their food materials. These latter are spoken of either as "facultative anaerobes" or "facultative aerobes," and among them are found the greater number of pathogenetic forms.

(*b*) **Relation to temperature.**—Bacterial growth extends over a wide range of temperature, but in the case of each variety there are definite limits between which alone multiplication can take place, and for each there is an optimum temperature most favourable to its growth. In general the upper limit of bacterial growth is about 40° to 45° C., though there are bacteria, the so-called "thermophilic" forms, which only begin to grow above this temperature and find their optimum between 60° and 70° C.

At the other end of the scale the lower limit is found at about 12° to 14° C., but forms exist which will develop even at 9° C., and find their optimum about 12° C. (psycrophilic forms). In almost all bacteria the effect of cold is merely to arrest development without producing permanent injury. Even a delicate organism like the cholera vibrio recovers perfectly after being cooled to −32° C., and a number of bacteria have been subjected to a temperature below −200° C. without suffering any apparent injury.

The optimum temperature may be found about 20°-28° C., as in the case of putrefa

forms; or about 37°-39° C., as in the case more particularly of the pathogenetic forms which attack warm-blooded animals and man.

The effect of high temperatures upon bacterial life is rapidly destructive, but its rate of action is to a great extent dependent on the accompanying conditions. It varies with the presence or absence of moisture in the bacterial surroundings, as well as with the manner in which heat is applied—whether in the form of hot air, boiling, or steam. Moreover, the degree of heat required to destroy bacterial life varies very greatly not only in the case of different micro-organisms, but, especially among spore-forming varieties, with the presence or absence of spores. Short of actual destruction of the bacteria, a raised temperature inhibits growth, and frequently modifies the character and the activity of the organisms concerned; as, for example, by causing loss of virulence in pathogenetic forms, loss of spore-formation in some spore-bearing varieties, loss of the pigment-forming power in pigmented organisms, and similar changes.

The action of hot air is considerably less rapid and less penetrating than that of moist heat, bacteria when dry withstanding a higher degree of heat, and a longer application of it, than when in a moist condition. Thus, while the spores of *B. anthracis* are destroyed in a few minutes by boiling, they will resist the action of hot air at a temperature of 140° C. for several hours. Experience shows that where hot air is employed it must have a temperature of 150°-170° C., and be applied for about three-quarters of an hour, to ensure the destruction of resistant spores.

Boiling, then, is more effective than hot air at the same temperature, and an exposure to boiling water for half an hour is sufficient to kill off not only all vegetative forms of bacterial life, but also the majority of spores. Some spores, however—for example, many which are commonly present in the soil—can withstand several hours of boiling. The addition of various salts, which raise the boiling-point, naturally renders the action of boiling water more effective This is important in the case of instruments and metal apparatus, where the addition of sodium biborate (or sodium bicarbonate), for example, not only ensures more certain sterilization, but at the same time possesses the advantage of preserving the metal from rust. Where water cannot be employed, heating in oil or glycerine is often used. But here it must be remembered that in the absence of water the effect obtained will be no more than if the organisms had been heated in dry air for the same length of time. This has been clearly established by direct experimentation.

Steam, owing to its greater penetrating power and more rapid conveyance of heat, is a more efficient agent than boiling water for bacterial destruction, and when pure steam is applied under increased pressure (as in an autoclave) very rapid effects are obtained.

Thus, while certain spores can withstand the action of steam at ordinary pressure for some hours, they are killed in a few minutes by super-heated steam at 120° C. (2 atmospheres pressure).

(*c*) **Other physical conditions.**—Under this heading are included the effects of radiant energy, electricity, and atmospheric pressure.

(1) *Radiant energy—light.*—To bacteria in general, light is not only not essential, but in most cases it is extremely harmful. Whether its presence is necessary to any bacterial forms is still in doubt. The destructive action of light upon bacterial life varies with its intensity and quality. Thus, while ordinary diffused daylight acts comparatively slowly, direct sunlight and strong artificial light (the electric arc) are rapidly destructive even when they have been entirely freed from heat rays. It is especially the rays of shorter wave-length at the blue-violet end of the spectrum which exhibit great bactericidal action, while the longer rays (yellow, orange, and red) have very little, if any, action As in the case of heat, the rate of action of light also is dependent on the presence or absence of moisture, and on the general composition of the medium. In illustration of the enormous power of intense light it may be mentioned that the *B. prodigiosus* exposed in a drop of fluid to a cooled arc light concentrated by quartz lenses is killed within about one second.

Röntgen rays and radium emanations both exhibit destructive action on bacteria under experimental conditions. It must, however, be clearly understood that neither in these cases nor in the case of light are the beneficial therapeutic effects of these agencies in any way dependent on their bactericidal power. They are entirely attributable to the tissue reaction which their application induces, and not to a direct destruction of the bacteria lying within the tissues.

(2) *Electricity.*—Electric currents (both continuous and alternating) were formerly supposed to exert an injurious influence on bacterial life. More recently, however, it has been held that the effects described were entirely indirect, and resulted from electrolytic liberation of strong chemical disinfectants (e.g. hydrogen peroxide). It was asserted that if non-polarizable electrodes were employed, these effects were not seen. But the latest investigations, carried out by Beattie and others, seem to indicate that electric currents of sufficient voltage have *per se* a destructive effect on many micro-organisms.

(3) *Atmospheric pressure.*—This is a matter of relative indifference to bacteria. They may be exposed in culture to a pressure of several hundred atmospheres without apparent injury.

(*d*) **Lack of food and moisture.**—Different micro-organisms vary greatly in their resistance to the unfavourable influences of lack of food and moisture. Thus, the cholera vibrio, for example, dies in two or three hours when subjected to drying, while other organ-

isms such as the *Staphylococcus pyogenes* and the *B. tuberculosis* can survive the process for many months at the least. Even such bacilli as the diphtheria and typhoid organisms, which are in general somewhat delicate forms, easily destroyed by other influences, survive drying for considerable periods. When dried in particular materials (e.g. pus, sputum, blood) they may remain alive and virulent for weeks, or even longer. The spore-forming organisms are naturally the most resistant to starvation and drying, and may preserve their vitality and their virulence for years under these conditions.

(*e*) **Action of chemical agents.**—In the case of food materials it is frequently found that substances which are even essential, or at any rate useful, and it may be actually stimulating to the growth of bacteria when present in certain proportions, will, when excessive in amount, inhibit growth or even destroy life. Thus, common salt, which is of extreme importance in the composition of culture media, will, if its percentage be unduly increased, give rise to the production of involution-forms, inhibit growth, and finally cause the death of the organisms concerned. Sugar, again, a natural foodstuff for many bacteria, will, as its concentration is increased, produce similar results. This kind of action may probably be attributed, in great part at any rate, to plasmolysis of the bacteria from alterations in osmotic pressure, for, in the case of other food materials whose concentration does not markedly affect osmotic pressure (e g. ordinary proteins), no such results accompany the presence of increased percentages.

Among substances other than food materials which require to be considered are not only those which are so directly inimical to bacterial life that they are classed as antiseptics, but also the various products of the metabolic activity of the bacteria themselves. These latter are often unfavourable to the continued life not only of the micro-organisms which produced them, but also of other varieties. On the other hand, some of the metabolic substances in question may, under certain conditions, act favourably on the growth of other micro-organisms, and even be essential to their nutrition.

Antiseptics are those substances which, even in relatively small amounts, are definitely injurious to bacterial life. Their effect may be due to their special action as protoplasmic poisons, as oxidizing agents, or as coagulants, and the like; or, more commonly, it is due to a combination of these properties. Their action naturally depends in a marked degree not only on the concentration in which they are present, but also on the manner and the vehicle in which they are applied. Factors of particular importance in this relation are the temperature, the reaction of the medium, the presence of greater or less amounts of colloid matter (e.g. proteins), the character and concentration of any inorganic salts which may be present, and so on.

The effect of any given antiseptic also *varies greatly with the micro-organism employed for testing it*, with the presence or absence of spores, with the age of the culture, and with the physical condition (e.g. dryness) of the bacteria exposed to its action. The form of the antiseptic itself, too, whether liquid or gaseous, has a considerable influence on its rate and mode of action. In the case of antiseptics in solution, the nature of the solvent has a marked effect on the results obtained, the most powerful action being usually exhibited by aqueous solutions, while *solutions in oil or in glycerine have a much smaller effect.*

The substances commonly employed as antiseptics belong to many different classes of chemical agents, including heavy metals, halogens, organic and inorganic salts and acids, and bodies of the aromatic series. Accordingly, it is impossible to enter here into precise details as to their probable mode of action on bacteria, beyond stating that their molecular weight and the degree of chemical dissociation which occurs in their solutions appear to bear an important relation to their antiseptic action. Beyond this, very little is actually known with certainty as to the influence of chemical constitution on antiseptic action. The action is undoubtedly a very complex one, and conclusions as to the value of particular antiseptics for particular purposes cannot be drawn with certainty from mere test-tube experiments. Thus, corrosive sublimate is a most powerful bacterial poison when dissolved in water, but in the presence of albuminous fluids, such as blood-serum, its effect may be reduced to as little as a hundredth part or less of its action in water. This result is no doubt owing to *the formation of mercury albuminates in the fluid and the consequent removal of much of the free antiseptic from the solution.*

Again, many antiseptic substances which prevent bacterial growth, even when present only in minute amounts, exhibit very little bactericidal power unless they act in relatively very strong solutions; while others, which cause much less inhibition of growth in weak solutions, are powerfully destructive of the bacteria when their strength is only very moderately increased.

Where animal tissues are concerned it will *frequently be found that the milder antiseptics give the best practical results*, since they inhibit multiplication of bacteria without causing injury to the tissues; whereas strong antiseptics may cause tissue injury and cell necrosis, and produce coagulation of albumin in the tissue fluids, thus shutting in the micro-organisms and protecting them from further antiseptic action.

(*f*) **Symbiosis and antibiosis.**—It has already been stated that the products of bacterial metabolism may be unfavourable or favourable to bacterial life. On the whole, such products act unfavourably on the growth both of the micro-organism which forms them and of other varieties; but in some cases the presence and activity of particular

bacteria improves the conditions for others, or actually makes existence possible for them where it would otherwise be difficult or impossible. Such relations between different bacterial forms are commonly spoken of as examples of symbiosis (e.g. the spirillum and bacillus of Vincent's angina), whereas the cases of antagonism or harmful influence are referred to under the term antibiosis.

The modern use of the Yogurth bacillus (lactic-acid fermentation) to check the growth of intestinal micro-organisms which produce injurious substances, affords an excellent example of antibiosis. Other examples in laboratory experience are found in the overgrowth and destruction of pathogenetic bacteria by putrefactive organisms or other saprophytic forms. On the other hand, instances of favourable action may be found where one series of micro-organisms produces substances which prepare or actually constitute the food material for other forms; or where aerobic micro-organisms, by removing oxygen, render it possible for anaerobic forms to grow. Thus, *B. tetani* appears to flourish best in a wound which has an additional infection with aerobic organisms.

2. VITAL PROCESSES

i. **Assimilation and dissimilation.**—The bacteria, though belonging to the lowest and most primitive forms of life, exhibit highly developed metabolic functions. The single tiny cells possess almost all the potentialities distributed in different organs in the more highly developed forms of life. The investigation of their vital processes is consequently all the more difficult and uncertain. Some of them find their food material in the simplest substances, and can build up highly complex protein compounds by a series of unknown syntheses from these elementary sources. Thus, certain forms can live and multiply when supplied with inorganic substances alone (carbon dioxide, ammonia, nitrates); others require organic nourishment of a simple kind (e.g tartrates); while the majority only carry on their metabolism when supplied with highly complex food materials (such as proteins or carbohydrates). They exhibit a remarkable activity in the processes of assimilation and dissimilation, and obtain the energy required for their elaborate syntheses from the decompositions and oxidations which they carry on within their protoplasm, or which they bring about in the surrounding medium by enzymic action.

ii. **Respiration.**—Aerobic bacteria, which require free oxygen in order to carry on their normal oxidations, may be regarded as exhibiting the phenomenon of respiration. They take up oxygen from solution in direct proportion to the activity of their growth and development, and give off carbon dioxide in corresponding

(though not equal) amounts. The excess of oxygen intake over the discharge of carbon dioxide is to be attributed to other oxidative processes which occur in the course of their metabolism, as, for example, the formation of water. The anaerobic forms which cannot use free oxygen, and are indeed inhibited by its presence, obtain the oxygen which they require for their life processes from the decomposition products of their food supply, and do not, therefore, exhibit respiration in the ordinary sense.

iii. **Heat production.** — The oxidations and decompositions carried on by the bacterial protoplasm result in the liberation of chemical energy, a great part of which is doubtless used in building up fresh protoplasm from the food materials, as well as in elaborating special substances, but part of it may appear in the form of heat. This is well seen in the case of ordinary putrefaction, and in the action of thermophilic bacteria in connexion with the smoking of dung-heaps and garden hotbeds, and in the heating of haystacks, which at times results in actual ignition.

iv. **Light production and phosphorescence.**—Some bacteria ("photobacteria"), of which the majority belong to the marine flora, exhibit the phenomenon of light production, and are often the cause of the phosphorescence of the sea and of that of decaying animal and vegetable matter. They only exhibit phosphorescence when alive and active, in the presence of oxygen, and under suitable conditions of temperature.

v. **Metabolic products.**—The products of bacterial activity are very numerous and varied. Some are more or less simple bodies of known chemical composition, and include gases, such as hydrogen, sulphuretted hydrogen, carbon dioxide, ammonia, and methane; inorganic substances, such as water, nitrates, chlorides, and so on; alcohols, acids, of the fatty acid and oxy-acid series; aromatic bodies, such as phenol, indol, etc.; and carbohydrates (e.g. sugar). Others are complex organic bodies of unknown constitution, such as the various pigments, enzymes, toxins, and so forth. These latter are the more important from a pathological aspect in that they include those bodies to which the special action of bacteria in the animal organism is attributable. In regard to many of these substances, we do not know with certainty whether they should be classed as secretions or as excretions of the bacterial protoplasm, whether they are formed within or without the bacterial cell, nor whether they are liberated by the living organism or are only set free when the cell itself undergoes disintegration.

(a) The **pigments** usually consist of more or less indifferent substances, and therefore are in general of comparatively slight importance among the metabolic products of bacteria, except in so far as they

assist us in the differentiation of bacterial forms which may otherwise present closely similar appearances. But in the case of certain of the bacteria in which the pigment is intracellular (e g. *sulphur-bacteria*) this substance is essential to the life of the organism, enabling it to assimilate carbon dioxide in the presence of light in the same way that chlorophyll assists the metabolism of higher plants. Where the pigment is extracellular it may probably be regarded as an excrete product of no particular importance to the bacterium. But even in these cases it is conceivable that, by absorbing light, pigment may either act protectively by taking up the more actinic rays, which are particularly injurious to bacterial life; or, on the other hand, it may assist bacterial growth by rendering the energy of light available in the assimilative processes. However this may be, it is a striking fact that the production of extracellular pigment is not *invariably* associated with the growth of the organism concerned, but frequently depends on the accompanying conditions of temperature, gaseous environment, medium, reaction, and so on. Thus the *B. pyocyaneus*, which exhibits a blue-green fluorescent pigmentation in agar, gelatin, or bouillon, forms a brown film upon the surface of a boiled potato. The *B. prodigiosus*, grown at about room temperature (15° C. to 20° C.), forms a bright crimson-red pigment, but when grown at 37° C. shows no coloration, and only gradually, if at all, reacquires the property of forming pigment on returning to the more suitable conditions. In almost all cases the pigmented organisms only exhibit their colour when oxygen is present, although the essential pigmentary substance must actually be formed even in its absence, and probably then exists in the form of a leuco-product, since the colour rapidly appears on the admission of oxygen.

(*b*) Enzymes.—The bacteria depend to a great extent, not only for their normal assimilation, but also for a large part of their pathogenetic action in the invaded organism, upon the effects produced in their surroundings by enzymes which they elaborate, and either retain within their protoplasm or discharge externally. Recent investigation tends to the conclusion that the setting-free of enzymes into the surrounding medium is to a great extent dependent on the disintegration of the bacteria themselves. And it is clear that all such enzymes certainly arise within the protoplasm of the cell itself, since they can be obtained from the bodies of the washed bacteria by submitting them to a sufficiently high pressure.

The effects of the zymogenetic action of bacteria fall into different groups according to the nature of the chemical changes produced. They may be broadly classed as processes of oxidation, hydrolysis, reduction, decomposition, and synthesis, as well as physical changes like coagulation, or a combination of several of these actions, as in

the case of fermentation and putrefaction. Oxidation occurs in the production of acetic acid from ethyl alcohol by the *B. aceti* (*Mycoderma aceti*), and in the formation of nitrites and nitrates from ammonia by the nitrifying bacteria. Hydrolysis is seen in the breaking-up of cellulose by the *B. amylobacter* (*Clostridium butyricum*) with a production of glucose; or of urea into ammonium carbonate, as, for example, by the *Micrococcus ureæ*; and in a great number of other well-known instances, among which may be mentioned the splitting-up of higher proteins into lower members of the group by peptic and tryptic action. Reduction is seen in the denitrifying action exhibited by a number of bacteria which reconvert nitrates into nitrites, and these again into ammonia and free nitrogen. Decomposition implies deep-seated changes in the structure of the molecules attacked, and is exhibited in the production of indol, fatty acids, amides, and many other bodies from albuminous matter.

(*c*) The **toxins** are the most important products of the action of pathogenetic bacteria. They are bodies of entirely unknown composition, but appear to be either colloids, or at any rate closely associated with colloidal matter, and are produced by the specific action of particular micro-organisms. Those of diphtheria, tetanus, and anthrax have been the most carefully studied, and their formation under artificial conditions has been found to be associated with the production of albumoses in the culture-fluid. If these albumoses are precipitated from solution, the toxic properties are found to accompany the precipitate. But that the albumoses are not actually the toxins is believed to be shown by experiments in which the precipitation of bouillon cultures with zinc chloride yielded bodies possessing characteristic toxic action, but exhibiting none of the reactions of protein in the dilution in which they were then tested. Moreover, if the bacteria are grown in media which contain no protein material, they are still capable of forming toxins. It must, however, be remembered that the bacteria themselves build up proteins from the food material supplied to them, and traces of protein actually make their appearance in these fluids along with the toxins. The toxins formed by the bacteria may either diffuse into the surrounding medium, or may remain within the cell, and only pass out into the medium on the disintegration of the cell itself. This observation has led to an attempt to classify bacterial toxins as either "intracellular" or "extracellular." But the farther knowledge advances the more difficult it becomes to uphold this distinction between the so-called "endotoxins" and the "exotoxins," since it seems probable that in every case the actual formation of the specific poison is an intracellular process.

Among the toxins formed by pathogenetic bacteria, some are

definitely specific, and exhibit a well-marked and characteristic action in the living body. Thus, tetanus toxin has a selective action on the central nervous system, producing irritation and tetanic muscular spasms, while the toxin of diphtheria attacks peripheral nerves and leads to paralysis. Other toxins produce more general results—disorder of metabolism, fever, and degeneration in parenchymatous organs—without possessing such defined effects as would distinguish clearly the particular infection.

Bacterial toxins are remarkable for their extreme potency in quantities quite minute as compared with active doses of the strongest known alkaloids. Thus, tetanus toxin may be prepared in a form several hundred times as powerful in its action as strychnine. Besides their proper toxins, pathogenetic bacteria produce in dead and decomposing animal matter poisonous bodies similar to the toxic substances produced by various saprophytes. The substances in question are called ptomaines, and are frequently of practical importance in that they may give rise to the severest symptoms of intoxication. They are distinguished from true toxins by their greater heat-resisting power, and they appear to be most nearly allied in constitution to the vegetable alkaloids. The general effects and mode of action of the bacterial toxins are dealt with further in the discussion of Pathogenetic Action and Immunity, p. 26 *et seq.*

vi. **Motility.**—The property of independent movement is enjoyed by many bacteria These are chiefly found among the vibrios and the rod-shaped organisms; indeed, it is doubtful whether any cocci possess motility, though the contrary has been maintained in certain cases (e.g. *Micrococcus melitensis*).

The movement is in general one of progression, the organism advancing in a definite direction for a period. It may then be observed to turn off at an angle, or to stop and remain at rest, or to move backwards in the reverse direction, or in other cases to turn round and retrace its path, until some new influence again arrests or modifies its movement.

Associated with the movement of progression, or independently of it, the organism may exhibit a rotation on its axis, and this in different cases may be either alternating—now in the direction of the hands of a watch, now in the opposite direction—or it may be limited, as in the spirilla, to one direction only, the micro-organism rotating always either to the right or to the left according as the screw of its spiral is right- or left-handed. The rate of movement varies greatly in the different motile forms, some moving with a remarkable rapidity (as much as twenty or thirty times their own length in a single second), while in others the motion is extremely slow, so that it is often difficult to distinguish it at all. The activity

of movement is *dependent in a high degree* on the conditions which surround the micro-organisms, and is particularly affected by the temperature, the gaseous environment, and the concentration of the medium in respect of salts. Moreover, wide differences in motility exist between different individuals in the same culture, some being highly active, while others are very sluggish or may be apparently quite non-motile. The latter may even yield a temporarily non-motile population in subculture.

The motility of bacteria is of considerabe importance in connexion with the study of the phenomenon of chemiotaxis.

vii. **Chemiotaxis.**—Under this term may be included a variety of similar phenomena exhibited by bacteria under the action of chemical substances, of light of different colours, of gases, of electric currents and the like. They depend on a definite attraction or repulsion of the organisms by the agency in question, which is expressed in the terms "positive" and "negative" chemiotactic action.

Though it might at first appear from some experiments that this special action of different substances on bacteria is a qualitative one, it is found on more exact investigation that in the greater number of cases, at any rate, the difference is really only quantitative, and that the attraction or repulsion of the organisms depends upon the strength and concentration of the agent under investigation. Thus, if a particular substance in solution is found to attract certain bacteria in a given concentration, then as its concentration is increased the attraction will gradually increase to a maximum. Further increase of strength beyond this point will lead to progressively diminishing attraction, and finally to definite repulsion, of the organism concerned. So far as present knowledge goes, it is impossible to establish any *general* relation between the chemical constitution or the nutritive value to the bacteria of the substances employed and the character of the chemiotaxis which results. Thus it may be found that valuable food-stuffs (e.g. sugar) may exert only the slightest positive action or none at all, while many substances which are distinctly harmful, and perhaps even destructive, to bacterial life, exhibit a definite positive chemiotaxis (e.g. salts of mercury and other heavy metals). In the case of light of different colours, and of various gases (e.g. oxygen at different partial pressures), the chemiotactic action would [illegible]ar to be more closely related to the favourable or unfavourable [illegible] the micro-organisms concerned of the various rays or gas[illegible] under observation, so that the [illegible] are found to [illegible] region of those light-rays or [illegible]ar oxygen-te[illegible] is most favourable to their de[illegible] growth.

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the phagocytic cells within the animal body. Between the latter and invading micro-organisms there appears to be strong mutual chemiotaxis (positive or negative), which is of great importance from its bearing on the phenomena of local inflammation (emigration of leucocytes, etc.) and infection in general, and in relation to the development of immunity.

3. DISTRIBUTION OF BACTERIA IN NATURE

In discussing the distribution of bacteria in a work on surgery, attention must naturally be directed chiefly to the pathogenetic forms. But the saprophytes also require consideration in this connexion, since a number of them may invade a surgical lesion, as, for example, a suppurating wound, and assist the progress of the pyogenetic organisms either by forming or removing particular substances, or by producing decomposition in necrotic tissues. Thus, aerobic saprophytes may enable anaerobic pathogenetic bacteria (e g in tetanus) to obtain a foothold by removing oxygen, and many of the toxic symptoms of moist gangrene, for example, may be attributed to the action of substances produced in the dead tissues by bacteria of putrefaction. Moreover, the presence of a large number of saprophytic forms in any given situation is a valuable indicator which should at once suggest the possibility that pathogenetic organisms may also be present, as, for example, in the air of an operating theatre.

Bacteria as they occur in nature are to be found in fluids of different kinds, and especially water, in the soil, in the substance and upon the surface of solid bodies, and in the air. In the air their presence is in one sense merely accidental, and is due to their being carried up in dust, or in the fine spray from splashing fluids, or discharged into it from the mouth and air-passages of animals or man in coughing, sneezing, or vocalization. It forms no part of their natural habitat, and yields for the most part chiefly such bacterial forms as offer a considerable resistance to drying. In the case of inhabited rooms and houses, however, a variety of pathogenetic forms, including the less resistant kinds, are often present, since the air receives continual fresh infections from the saliva sprayed into it in speaking. This is a point of special importance to the operating surgeon who, while observing every possible precaution to secure pure air in his operating theatre, may inadvertently infect the site of operation in speaking if his mouth is not properly screened, since quite healthy persons frequently carry in their mouths organisms which may be virulent to another individual (e.g. streptococcus, pneumococcus, staphylococcus, etc.).

As micro-organisms suspended in the air are subjected to continued drying, the bacteria of chief importance from the standpoint of aerial

infection (apart from the special case of salivary infection already dealt with) are those which can resist the effects of drying most successfully. Such resistance is dependent either on particular characters of the bacterial protoplasm or envelope, as in *B. tuberculosis*, or on the faculty of forming spores, as in *B. anthracis*.

The bacteria found in water are of relatively small importance in surgery, as the majority of them are harmless saprophytes, and those pathogenetic forms which do occur from time to time belong chiefly to the less resistant varieties, and are easily destroyed by a few minutes' boiling. They reach the water by being washed down from the soil by rain, by the discharge of sewage into rivers, and the like. Here they are exposed to the struggle for existence with the natural bacterial flora of the water, as well as to other harmful influences, such as the destructive action of sunlight, which indeed is one of the chief factors in the so-called self-cleansing of rivers.

Sea-water may be regarded as being practically free from bacteria which are pathogenetic for man, as soon, at any rate, as open water is reached. But near the shore, especially in bays and at the mouths of rivers, there may be almost as many pathogenetic micro-organisms as in the water of a dirty river itself. Thus, in the waters of the Bay of Naples, for example, the *B. typhosus* among others has been met with.

In soil a great number of micro-organisms are to be found, and among them are various pathogenetic forms, some of which, for example the *B. tetani*, the *B welchii*, and the *B. œdematis maligni*, find their natural habitat in the surface layers of cultivated ground. Others which do not naturally belong to the flora of the soil can exist in it for longer or shorter periods, especially if they belong to the spore-forming bacteria (e.g. *B. anthracis*). Besides these, where the soil has been contaminated by the excretions or dead bodies of animals or man almost all the pathogenetic bacteria may be met with, and may occasion infection under suitable conditions.

The bacteria found in soil are consequently of great importance in surgical pathology, not only from their number, and the ease with which many of them may infect the body, as for example *B. tuberculosis*, *B. typhosus*, the pathogenetic cocci and *B. diphtheriæ*, but also because they include some of the most virulent and most resistant forms, namely, the tetanus bacillus and the organisms of the malignant œdema group. To their anaerobic nature must be attributed the comparative rarity, under ordinary conditions, of wound infection with these micro-organisms, considering the wideness of their distribution and the frequency of lesions exposed to direct soil contamination. It would appear that they are only able to develop in the animal body where they are sheltered from oxygen by the presence

of dead tissue (e g. in extensive lacerated wounds), or by the action of other (aerobic) micro-organisms, which by taking up the oxygen produce conditions suitable for anaerobiosis. The great majority of the bacteria of soil are, however, pure saprophytes. Below the surface layers at a depth of a few yards in the subsoil no bacteria are to be found. The deeper parts of the soil contain no suitable material for their growth, and the soil itself acts as an efficient filter for bacteria, except where definite cracks permit their carriage downwards by the percolation of water from the surface of the ground.

In or upon the surface of the animal body a vast number of bacteria, pathogenetic and otherwise, find the most favourable conditions for their growth in the presence of suitable moisture, temperature, and nourishment. The skin and mucous surfaces form an admirable collecting ground for bacteria, in which they flourish under the protection afforded them by irregularities of the surface, by ducts and glands of different kinds, and by crypts and follicles, where they can live and multiply in favourable surroundings, and from which it is extremely difficult or impossible to remove them by any process of cleansing.

More than one hundred different varieties of bacteria have been shown to occur upon the skin in man. And in the mouth, the nasal passages, and the intestine is constantly to be found an abundant flora. Many of these organisms continue to exist on the healthy and unbroken surfaces as harmless saprophytes, but may take on pathogenetic action if they gain an entrance to the tissues through some injury. Moreover, if transferred to another individual, an organism which was quite harmless to its original host, or had become so by the lapse of time, may develop active pathogenesis, as in infections conveyed by "carriers" of typhoid, dysentery, diphtheria, or cerebro-spinal meningitis.

The different surfaces of the human body have each to some extent their own peculiar flora. Thus, on the skin the staphylococcus albus is invariably present; in the mouth, spirochætes, streptococci, and streptothriceæ among others are always found; in the intestines, *Bacillus coli*, *B. lactis aerogenes*, and streptococci (*S. fæcalis*) are normal inhabitants; and in the healthy vagina *B. vaginalis* is a characteristic organism. But, besides these more or less normal constant residents, numerous pathogenetic forms may occur upon the skin, as, for example, pyogenetic cocci and *B. pyocyaneus*. In the mouth and nose pyogenetic organisms are common, and the Pneumococcus, *B. influenzæ*, *B. diphtheriæ*, and *Micrococcus intracellularis meningitidis* may be met with, in addition to the organisms definitely connected with special diseased conditions of the mouth and nasal cavities, as, for example, those associated with rhinoscleroma and fetid ozæna. The actual substance of the tissues and organs of the body is normally

sterile, as are also the urinary and genital passages, except in the neighbourhood of their external openings (e.g. urethra and vagina).

From the surgical standpoint it is important to remember that though the surface of the skin may, and indeed must always, be most carefully cleansed before any operation, it is impossible to maintain it in an absolutely sterile condition, since the glands and ducts harbour large numbers of micro-organisms which cannot be removed. These may be *rendered active* if the skin be unduly irritated in the process of preparation, or bruised in the course of the operative procedures. For the same reason the surgeon's hands, which may be absolutely sterile (on the surface) at the beginning of an operation, are gloved because they will cease to be sterile when his manipulations have brought out the secretions present in his sudatory and sebaceous glands. As a rule the micro-organisms likely to be thus conveyed into the wound are of comparatively slight importance owing to their low virulence, but their presence probably explains the occurrence of the mild suppurations which are sometimes seen even after operations conducted under the most favourable conditions.

In the case more especially of the less virulent bacteria the number present is a factor of very great importance in determining the production of suppurative inflammation. On this account, although it is impossible *entirely to cleanse such sites of operation* as the mouth, or nose, or the intestinal tract, yet it is desirable before operation in these regions, to reduce the number of micro-organisms present, so far as possible, by non-irritating methods. In the case of the intestine, for example, it is possible by combining large doses of bismuth salicylate with the usual aperient and enema, and giving only sterilized soft food for a couple of days, so far to cleanse the intestinal tract that the danger of peritoneal infection is enormously reduced.

C. PATHOGENETIC ACTION OF BACTERIA

1. MODES OF INVASION

Except in the relatively infrequent cases where, either as the result of accident or from the bites of insects, infective micro-organisms are introduced directly into the blood-stream, infection always begins as a localized phenomenon, and leads to the production of a more or less distinct and definite local inflammation. Subsequent spread may lead to the dissemination of the infective agent through the body, with the production of general disturbances and the formation of secondary foci of infection. Or, apart from the spread of the micro-organisms themselves, the local production of toxic substances and their diffusion through the body in the circulating fluids may lead to severe general intoxication.

In the case of the best-known specific infections the micro-organisms usually enter by one of the mucous surfaces (e.g. respiratory, alimentary), except in the case of tetanus and hydrophobia, which are wound infections, of syphilis, where the infection usually gains an entrance through some slight abrasion, and of the "fly inoculations" (malaria, yellow fever, plague, and trypanosomiasis). Ordinary pyogenetic organisms usually enter by wounds, ulcerations, or abrasions of the body surface.

2. MODES OF SPREAD

The commonest and most natural mode of spread of infecting micro-organisms is by continuity of tissue either in the substance of an organ or along a surface. Along the mucous surfaces the spread is naturally most usual and most rapid in the direction of the normal flow of fluid. Discontinuous spread may also occur along the natural passages of the body, as, for example, when sputum from a tuberculous lung is swallowed and infects the alimentary canal, or when the gall-bladder is infected from the intestine without the bile-duct being involved in the inflammation. General dissemination of the infection is brought about by the escape of micro-organisms into the lymphatic circulation or the blood-stream.

It must also be remembered that the phagocytes themselves may actually assist in spreading an infection by carrying off micro-organisms in their bodies, and being subsequently destroyed by the bacteria, which are then free to multiply in their new situation.

Other modes of spread that may be mentioned are by rupture of an abscess into a body cavity or blood-vessel, by transference along the perineural lymphatics, or by passage along the lymphatics from an infected area to reach a body cavity or lymphatic space, as, for example, from the auditory or the nasal passages to the meninges of the brain.

3. ACTION OF PATHOGENETIC MICRO-ORGANISMS

The mode of action of invading micro-organisms on the tissues of the body must of necessity be either mechanical or chemical in character. The former is of relatively slight importance owing to the minute size of the organisms in question. When they are massed together in enormous numbers they may succeed in forming capillary emboli. But in the vast majority of cases of infective embolism it is detached blood-clot containing bacteria, not the bacteria themselves, which causes the obstruction.

The chemical action of the bacteria is by far the most important, and is due to the toxins and other poisonous bodies set free by the activity of the micro-organisms. These substances

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have already been described (under Metabolic Products, p. 18), and their effects are now briefly to be considered. They may be subdivided into local and general actions. The **local** effects are those of local irritation of varying degree, leading to more or less evident inflammatory reaction. This may be very slight indeed, as in some cases of tetanus infection, or it may be violent and extensive in character, and accompanied by marked destruction and degeneration of tissue, resulting in the formation of large centres of necrosis and suppuration.

The more **general** effects are those which depend upon the special action of the bacterial toxin circulating in the blood, and include tissue degenerations (especially cloudy swelling), disorder of metabolism, and *pyrexia*. *In some infections the specific toxins seem also* to possess a selective affinity for particular tissues, and produce in them their most characteristic effects. This may be seen, for example, in the action of tetanus toxin on the central nervous system, or in that of the diphtheria toxin on peripheral nerves.

In addition to the direct injurious action exerted on the tissues by invading micro-organisms and their toxic products, a number of extremely important phenomena occur in the course of an infection which are the expression of the reaction of the organism against the infective agents and their toxins. They are conveniently grouped together under the heading of immunity.

4. IMMUNITY

If a number of individuals be exposed to the same infection, it is usually to be observed that only a certain proportion of them develop the actual disease. Others may suffer from some temporary indisposition; while the remainder exhibit no symptoms at all. These facts present a striking illustration of the phenomenon of resistance to infection which is dependent either on a natural or on a previously acquired condition of immunity to the particular disease concerned. Such immunity may be regarded as antibacterial in character, or antitoxic, according as it is directed chiefly against the bacteria themselves or more especially against their toxic products. To the former class belongs immunity against the causal agents of enteric fever, cholera, bubonic plague, and anthrax, for example; to the latter, that against the toxins of diphtheria and tetanus.

The problems of resistance and reaction to infection may conveniently be dealt with under the headings of *natural* and *acquired immunity*.

Natural immunity.—This may be either absolute or relative, and the resistance to infection which it implies may be either racial or only individual in character. That is to say, in some cases a particular

species may possess immunity against a given infection, while in other instances it is a question only of a greater or less susceptibility among the individual members of a susceptible race. Thus, dogs are found to be immune to anthrax, man to cattle plague, and fowls to tetanus. On the other hand, man is susceptible to scarlet fever, for example; yet a certain proportion of men do not take the disease, although they may be frequently exposed to the infection. These statements hold good not only for bacterial diseases and the effects of micro-organisms and their toxins, but also for a number of other poisons of animal or vegetable origin, as, for example, snake venoms, to which pigs and hedgehogs are by nature insusceptible.

Acquired immunity.—Immunity may be acquired by susceptible individuals either *naturally*, as the result of a successful response to an acquired infection, thus leading to recovery from the disease; or *artificially*, as the result of inoculation with the specific micro-organisms themselves or with their products. Such immunity, resulting as it does from a definite reaction of the individual itself, is called "**active**" immunity, in order to distinguish it from the condition of "**passive**" immunity which may be temporarily induced by the introduction of protective substances obtained from actively immunized animals

The protective action exerted by the substances in question (e.g. blood-serum) has been shown to depend upon the presence in them of specific *antibodies* which have been produced within the actively immunized animal as the result of the reaction of its tissues to the specific causal agents of disease.

Substances which possess this faculty of giving rise to the formation of antibodies when injected into the body of a living animal are now usually spoken of as *antigens*, and include, besides bacteria and their specific products, a large number of other substances, such as blood-corpuscles, animal and vegetable cells, proteins, toxins, and venoms of animal or vegetable origin, enzymes and ferments, and so on. Their accurate study has thrown a flood of light upon many of the problems of antibacterial immunity, and has led to the discovery of a number of important facts bearing on the nature and properties of antibodies in general.

During the development of active immunity, besides the formation of antibodies under the influence of particular antigens, there is usually a remarkable increase in the number of leucocytes in the circulating blood, and also an increase in the phagocytic power of these leucocytes. The leucocytosis sometimes reaches a very high degree at certain stages of the reaction to infection, and leucocyte proliferation is by some observers held to be associated with the production of the antibodies. The increased phagocytic power of the leucocytes is itself

had not been destroyed by the antitoxin, but was merely kept inactive by being held in some kind of chemical combination or association with it.

That such a combination actually takes place has been denied. But the great mass of evidence available strongly supports the view that the antitoxin actually neutralizes the toxin in much the same way that an acid neutralizes a base. It would appear that it is in general only possible to recover toxin from a toxin-antitoxin mixture when the two have remained in contact only for a short time. When the combination has had time to become complete, neither by heating nor in any other way can the toxicity of the mixture again be restored.

Among the other immune substances produced in the course of the development of immunity some of the most important are the **agglutinins.** These bodies are produced more particularly in infections with such organisms as *B. typhosus*, *B. paratyphosus*, *B. coli communis*, *B. choleræ asiaticæ*, *B. dysenteriæ*, and the *Micrococcus melitensis*. They differ from the antitoxins in that they do not, to any great extent at least, affect the pathogenetic action of the bacteria in question, but produce a physical change in the condition of the organisms concerned. That is to say, they cause an aggregation of the bacteria into larger or smaller clumps, which in the case of living motile forms is preceded by a paralysis of motion. The vitality of the bacteria is not affected by the occurrence of agglutination, nor is this phenomenon in any way dependent on the vital activities of the organisms themselves, since it occurs equally well if the bacteria in suspension have previously been killed by suitable means.

The fact that a development of agglutinating substances in the blood-serum occurs in these infections has proved itself to be of practical account, and is of very great utility both in assisting and confirming the diagnosis. This is all the more the case since the agglutinins begin to appear at a very early stage in the disease—at a time when, in many instances, in the absence of successful isolation of the causal agent, the clinical diagnosis must necessarily otherwise remain in doubt.

When the production of agglutinins has once been established in a particular individual, evidence of agglutinating action may be found to persist for a long time, and in cases even for a number of years. In such a case, if the blood-serum be examined on several successive occasions its agglutinating power will be found [illegible] approximately *constant*; whereas, if the infection be a rec[illegible]ies of examinations of the blood will show marked diff[illegible]e amount of agglutinin present on [illegible]sions, since [illegible]ion undergoes a definite rise [illegible] the dev[illegible] cou[illegible] active immunity.

The **precipitins** are produced in response to the injection of various albuminous substances, and appear in the serum of the animal injected. When such immune serum is added to a solution of the particular albumin concerned, a precipitate is formed. The reaction can be applied to the differentiation of albuminous bodies, such, for example, as the proteins of blood in different animals, and has been used with advantage both in forensic medicine and in hygiene. It must, however, be remembered that the differences observed in testing different solutions of albumin are in many cases only quantitative. Consequently, a graduated series of quantitative observations, with adequate controls, is needed to give reliable results.

Bacteriolysins are produced by the inoculation of animals with the bodies of bacteria, whether living or dead, and are developed in the course of natural infections such as cholera, enteric fever, and the like. They cause disintegration of the bacterial cell. This action has been shown to depend upon the presence of two substances which work together, the one being of the nature of a specific antibody (*immune body* or *amboceptor*), the other the thermolabile non-specific substance already mentioned, called the *complement*, which is rendered inactive by heating for one-half to one hour at a temperature of about 55° C. Bacteriolysis can only be produced, either in the animal body or *in vitro*, when both these substances are present.

The injection into animals of alien red blood-corpuscles leads in a similar manner to the development of specific *hæmolysins* in which the same thermolabile non-specific complement, always present, though in varying amount, in the fresh blood-serum and other body fluids, unites in action with a specific antibody to bring about the solution of the red blood-corpuscles in question. These hæmolysins, whose action seems to be entirely comparable to that of the bacteriolysins, have been of the utmost value in assisting the elucidation of the phenomena of bacteriolysis

Bacteriolysis can be followed either *in vitro*, when it is necessary to supply complement for the reaction as well as immune body, or in the peritoneal cavity of a living animal, in which case the complement needed is supplied by the normal peritoneal fluid of the animal itself. The intraperitoneal experiment in the guinea-pig was studied more particularly by Pfeiffer, and is generally known as **Pfeiffer's reaction.** Besides its bearing on the general questions of immunity, it has great practical value in the differential diagnosis between *V. choleræ asiaticæ* and allied organisms.

Following up the problems presented by the study of hæmolysis and bacteriolysis, it has been found possible to produce an anticomplement by injecting alien normal serum into animals, and in some cases anti-immune bodies have also been obtained. The study of

anticomplement and the phenomenon of "complement fixati first observed by Bordet and Gengou, led indirectly to the disc of the so-called Wassermann reaction for the diagnosis of syph infection. This reaction depends on the prevention of the hæmo action of specific hæmolytic immune body and complement by serum of a syphilitic subject in the presence of a suitable an such as an extract of syphilitic liver or, better, an alcoholic ext of a normal heart. In this reaction the extract represents the ant and the syphilitic serum the specific syphilis antibody. When t are present together they take up and fix the complement w would otherwise produce hæmolysis in association with the spe hæmolysin. The test has met with a remarkable measure of succ and is of the greatest value in the diagnosis of syphilis in all sta Its theoretical basis is, however, still obscure.

In attempting to apply the results of the experimental invest tion of immunity to the treatment of infective disease, whethe man or in the lower animals, both *passive* and *active* immuniza have been extensively employed. In the passive method—ser therapy—immunity is sought to be conferred by the introduct into the patient of the antibodies present in the serum of immun animals, as, for example, in the antitoxins of diphtheria, plague, teta and anthrax. In the active method the patient is stimulated produce his own antibodies by inoculation with a vaccine prepa from the actual causal agents of the disease itself.

Anaphylaxis.—The phenomenon of *anaphylaxis*—or *allergy*, a is frequently termed when studied in relation to cutaneous reacti —was first investigated by Richet, though attention had alrea been drawn to manifestations of *supersensitiveness* by Koch's obser tion of the high susceptibility to tuberculin of tuberculous individua The subject sprang into importance with Theobald Smith's d covery of the fact that guinea-pigs which had been inoculated wi a balanced harmless mixture of diphtheria toxin and horse-ser antitoxin might die on injection at a later date with a dose of norm horse-serum. In man also, individuals who have been treated wi antitoxin may, on inoculation with serum on a later occasion, mar fest more or less grave constitutional disturbances, to which t name of *serum-sickness* was given by von Pirquet and Schick. It indeed stated that sudden death has on occasion followed the i jection of serum in persons remaining supersensitive from a previo dose.

Substances which on injection may give rise to a condition supersensitiveness are called *anaphylactogens*. So far as is know they are always proteins, and almost any soluble protein (excep gelatin) may act as an anaphylactogen. The anaphylactic conditio

is *specific* in the sense that the animal is rendered sensitive only to the particular protein or proteins injected (e.g. horse-serum); and the symptoms of anaphylactic shock indicate the existence of an intoxication. The poisonous agent is termed *anaphylatoxin*, and according to the view of Friedberger and others it is produced from the injected protein in the course of its partial decomposition or digestion in the body fluids. Thus, it is supposed that in response to the first inoculation of an anaphylactogen, antibodies are formed which, with the assistance of complement, gradually digest or break up the foreign protein, one or more of the products possessing toxic properties at some stage of the decomposition. On a second inoculation being made at a suitable interval of time, the reaction proceeds much more rapidly owing to previous establishment of antibody-formation. Hence, as Friedberger believes, a relatively large amount of anaphylatoxin is quickly formed in the blood, and intoxication or anaphylactic shock results.

The anaphylactic antibody is termed *anaphylactin*; and in support of his view Friedberger showed that if the precipitate produced by mixing serum containing the anaphylactogen with serum containing its anaphylactin be treated with complement *in vitro*, anaphylatoxin is produced.

It has also been found that the serum of an anaphylactized animal will, when injected into another animal, produce *passive anaphylaxis*, rendering it supersensitive to the particular anaphylactogen concerned.

But if, as Friedberger holds, the union of anaphylactogen and anaphylactin which induces supersensitiveness is a union occurring in the blood, it is difficult to harmonize the phenomena of anaphylaxis with the well-ascertained facts of the normal development of immunity following inoculations of various kinds.

This difficulty is avoided in the view put forward by Dale and by Weil that anaphylactic shock does not occur when antibodies (anaphylactins) are present *in abundance* in the blood, and are able there to fix the anaphylactogen. According to these observers, the shock is induced only when anaphylactogen becomes attached to anaphylactin which is *anchored in cells*—that is to say, when there is not enough free anaphylactin in the blood to intercept and fix the anaphylactogen before it can reach the sensitive cells in quantity. The theory of Dale appears to offer a more satisfactory explanation of the facts at present known than the earlier view of Friedberger.

There is a tendency at the present time to explain a number of instances of supersensitiveness in man as belonging to the group of anaphylactic phenomena. Thus, "hay fever" due to the action of the pollen of various grasses; the susceptibility of particular

individuals to unpleasant effects from horse-dandruff, from the propinquity of cats and the like; certain forms of asthma; and the inability of some individuals to take particular foods without ill effects (e.g. strawberries, shell-fish, eggs), are regarded as examples of the anaphylactic state.

The principle of **vaccination against specific disease** was first placed upon a scientific basis by the work of Jenner in 1796. It was employed by Pasteur in his remarkable investigation of rabies, which culminated in the discovery of the extremely valuable method of treating that infection with which his name is always associated. More recently, and chiefly under the inspiration of Almroth Wright, the use of *vaccines* has rapidly been extended in the prophylaxis and treatment of a number of bacterial infections of known origin—for example, typhoid and paratyphoid infections, cholera, plague, tuberculosis, infections with pyogenetic micro-organisms, and the specific cocci (gonococcus, pneumococcus, etc.). In association with its practical application, the theory of the production of opsonins in the blood-serum during the development of immunity has been elaborated by Almroth Wright. Following the important observations carried out by Leishman on the degree of phagocytosis which occurs in the blood of patients suffering from infective disease as compared with that in normal healthy blood, he devised a method by which the "opsonizing" action of a patient's serum for a particular bacterium can be compared with that of the serum of a normal person (*see* under Technique, p. 52). The ratio obtained is called the *opsonic index*. It is believed to afford reliable information as to the degree of immunity attained by the individual under observation, and is made use of as a control and guide during his treatment by a series of inoculations with bacterial vaccine.

The practical value of this vaccine treatment is a question upon which judgment must still to some extent be held in suspense (*see* the next article).

D. TECHNIQUE

Those methods and manipulations are here described which the surgeon should be prepared to carry out for himself *as a matter of routine in his own* consulting-room or operating theatre. They include the best manner of [illegible] bacteriological investiga- [illegible] examination; and the [illegible] brief account is given [illegible] the sigma reaction in syphilis, and of the determination of the opsonic index.

A large amount of the material presented for examination to bacteriologists gives no result of value, and, indeed, could not be expected to give any in-

formation of importance, *owing to lack of attention to the few elementary principles which require to be remembered in collecting and transmitting specimens for examination.* It is, therefore, necessary to emphasize the observation of certain simple precautions in the handling of bacteriological material.

GENERAL METHOD FOR COLLECTING FLUIDS TO BE EXAMINED

Fluids must be collected without allowing the occurrence of *external contamination*, otherwise the subsequent examination will be entirely misleading.

If *small quantities* will suffice, the most convenient method is to draw out short capillary tubes or spindle-shaped tubes (Wright's capsules) from thin-walled glass tubing in a spirit-lamp or Bunsen burner. These are sterilized in the making, and when the fluid to be examined has been allowed to run into them the ends may be sealed up immediately.

Where *larger amounts* are required, sterile test-tubes should be employed. The usual cotton-wool plug (of non-absorbent wool) suffices if the tube can be kept upright and at once carried to a laboratory. But for transmission sterilized rubber stoppers[1] must be used instead of cotton-wool, to prevent leakage or evaporation of the fluid. If sterilized vessels are not available, a test-tube or small medicine-bottle and a suitable rubber stopper must be sterilized (by boiling for about 10 minutes) and then allowed to cool. This will ensure satisfactory results, except in the rare cases where highly resistant spores happen to be present, as, for example, on unused and newly unpacked glass, which should therefore be avoided The material to be examined should be *dispatched as soon as possible*, and should in the meantime be kept in a *cool* place and not unnecessarily exposed to light.

The quantity of fluid required for examination will depend to a great extent on the nature of the fluid, and on the micro-organisms to be sought for. A small quantity of pus, for example, will be sufficient for the discovery and identification of ordinary pyogenetic micro-organisms, while, on the other hand, in the case of urine or a serous exudate, not less than 100 c c. of fluid, at the least, should be available if the presence, for example, of *B. tuberculosis* is suspected

In all cases special care must be taken in collecting the fluid not to infect it from the skin or elsewhere. Otherwise the isolation and identification of the actual causal agent will be rendered difficult or even impossible, and the whole fluid may be overgrown by extraneous organisms. The presence of antiseptics must be carefully avoided, since they may entirely prevent the subsequent cultivation of the micro-organisms present.

Pus.—When possible, pus should be collected in a sterile syringe by puncture through the unbroken skin, after careful cleansing of the surface with ether and alcohol or painting with iodine. If this is undesirable or impracticable, the first portion of the pus should be allowed to flow away from an opened abscess, for example, before the sample is taken for examina-

[1] If rubber stoppers are not available, freshly boiled corks may be used. These ought preferably to have been previously autoclaved. The boiling not only sterilizes the corks but also makes it easier to fit them into the tubes.

tion. In the case of open suppurating wounds and sinuses, the superficial parts should first be cleansed with sterilized cotton-wool and sterile water (not an antiseptic), and the sample of pus obtained from the deeper part of the wounds where *contaminating saprophytic organisms are less likely* to have penetrated.

In some cases where there is relatively little pus and a long sinus or other open channel, the best results may often be obtained by freely irrigating the external portion, and then passing in a swab, like a diphtheria throat-swab, and carefully *swabbing over the walls of the cavity*. *At times* it may be necessary to leave such a swab in place for a quarter of an hour or so to soak up the discharge (e.g. in seeking for gonococci in the cervix uteri in chronic cases of gonorrhœal infection).

Blood.—In collecting blood it is important to secure a sufficient quantity to enable the examination *required to be carried out easily, and in* such a way as to give the most reliable results. For *agglutinin reactions* (Widal), it is best to take about 5 c.c. of blood from a vein with a sterile syringe, but in any case not less than 1 c c. of blood should be obtained. This smaller quantity can easily be taken either from the lobe of the ear or from the finger, by making a number of small pricks quite near together, with a fine needle-point, or even better with a sharply drawn-out bit of fine glass tubing. This method is both less painful to the patient and usually gives more blood than a single deeper prick. The finger or ear being previously cleansed, the blood is allowed to run into a spindle tube with capillary ends, or a dwarf test-tube 2½ in. long by ⅜ in. wide. When enough has been obtained, the spindle-shaped tube is sealed up, or the test-tube closed with a sterile rubber stopper, and set aside for the blood to coagulate. *The still too frequent practice of collecting the blood for a Widal reaction in a* capillary (vaccine) tube is to be strongly discouraged.

For the *syphilis reaction* (Wassermann's sero-diagnosis or the sigma reaction), 5 c.c. of blood will be required, and should be obtained by inserting a sterile dry syringe, preferably "all-glass," into a superficial vein *in the arm or hand. If the needle have a sufficient bore the blood* will flow into the syringe of itself, pushing the piston back. The use of anticoagulants is to be avoided, for there is no danger of the blood coagulating in the syringe *before* it can be transferred to a test-tube if the operation be properly performed, and the addition of these substances might interfere with the success of the subsequent examination.

If the blood is to be examined for the presence of *bacteria*, it is desirable to collect as much as 8 to 10 c c. by the same method. Less than this amount is insufficient to give reliable *results, as the bacteria may be relatively very few* in the peripheral circulation. The blood is at once transferred to a sterile vessel (e.g. test-tube), and may with advantage be defibrinated to keep it fluid by shaking it for some minutes with a few bits of glass, or tin tacks, or a little coil of galvanized iron wire inserted in the *vessel before it is sterilized*.

If the blood cannot at once be taken in hand by a bacteriologist, it should without delay be diluted about ten times with sterile distilled water or sterile normal saline solution in a sterile *flask, if sufficient culture bouillon*

for the purpose be not at hand. It is essential that the blood should not remain undiluted for any length of time, as the bactericidal substances set free in it might possibly suffice to render it sterile even if it originally contained a considerable number of living micro-organisms. This fact accounts for many otherwise inexplicable results which are obtained in the course of blood examinations.

Urine.—Urine should always be collected for bacteriological examination by catheter. In the case of females this rule should have no exception unless the examination has to be frequently repeated (e.g. in suspected tuberculosis). In the male, if a catheter cannot be passed, or its use is undesirable, the penis should be carefully cleansed, and the first portion of the urine allowed to escape, only the later flow being used for examination. Morning urine is always preferable for the purpose, if obtainable.

Where the urine is purulent, or obviously contains bacteria, a small amount will suffice for examination. But if it is to be searched for tubercle bacilli, a large quantity must be collected and carefully centrifugalized. The deposit is then examined.

Pleural and other fluids.—Similar considerations to those already mentioned apply to the investigation of pleural, cerebro-spinal, and other fluids.

Tissues.—Tissues removed for bacteriological investigation should be washed in a stream of sterile water, dried with sterile gauze or absorbent cotton-wool, and placed in a dry sterile test-tube or similar vessel closed with a rubber stopper for transmission to the laboratory.

MAKING OF CULTURES

Whenever practicable, it is important, in addition to the collecting of material for subsequent examination, that a culture should be made on the surface of a suitable medium (e.g. sloped-agar, blood-agar, or serum-agar) *without delay*. This should be done either with a platinum loop or needle, or by gently smearing over the surface of the medium with a small sterile cotton-wool swab which has been in contact with the infective material, care being taken not to break the surface of the agar.

If there is a probability of the presence of more than one variety of micro-organism, a separation may usually be effected without difficulty by the following method, using a series of three or four sloped-agar tubes. Take agar tubes which have been sloped long enough for the small amount of condensation water to collect at the foot With a platinum loop or needle infect the condensation water of the first tube from the material to be examined, taking care not to touch the surface of the agar. Sterilize the loop, and from the condensation water of tube 1 infect the condensation water of tube 2, and so on, care being taken in each case not to touch the surface of the agar with the loop. In this way a number of dilutions are made in the condensation water of the successive tubes. Now take each tube in hand successively, and run its condensation water over the surface of the slope, or spread it over carefully by means of a sterile platinum loop. The tubes may then be incubated in the upright position, and subsequently

one or more of them will exhibit well-isolated surface colonies from which subcultures and microscopic films may be made.

Instead of agar, *coagulated blood-serum* may be used for making cultures. It must *always* be employed for the diagnosis of diphtheria. The use of gelatin is undesirable in this kind of work owing to the low temperature at which it becomes liquid, a temperature much below that most favourable to the growth of the majority of pathogenetic micro-organisms.

Cultures thus made should be sent with the sample of pus or other material for examination, and are likely to prove of invaluable assistance to the bacteriologist in diagnosing the true character of the infection.

PREPARATION OF FILMS

In all cases, films for microscopical examination should be prepared *at once* from the material available, and should accompany any sample sent for examination. This is of special importance in the case of blood and other coagulable fluids, from which good films cannot be made after coagulation has been allowed to take place. Moreover, where bacteria are present, such a film gives a much more accurate idea, both of their absolute number and of the relative number of the different varieties where more than one variety occurs, than can be obtained in any other way.

In some instances the preparation of films may be all that is required to establish a diagnosis with sufficient certainty. Thus, in ordinary acute cases of urethritis, the presence of numerous organisms having the appearance of gonococci within the cells of the discharge will be enough to satisfy the surgeon; and, similarly, the detection of acid-fast bacilli in the sputum will usually justify a diagnosis of tuberculosis.

Method.—Films should by preference be made on microscope slides and *not* on cover-glasses. The latter are fragile and difficult to handle, while the former are much more convenient and safer, and have the advantage of giving a much larger film for examination. The slides must be carefully cleaned and freed from grease by means of acid alcohol (containing 1 per cent. HCl), and may then be kept in 96 per cent. alcohol. The film should be spread thinly and evenly over the surface, leaving at least one-quarter of the slide at one end free for holding. The pus or other material is spread uniformly in a thin layer on the slide, and then gently dried over a flame, or fixed with ether-alcohol mixture (ether one part, alcohol two parts).

Air-dried films are fixed by bringing the *back* of the slide down upon the flame of a Bunsen burner with repeated stroking movements, until it is so hot as to be only just bearable for an instant against the skin of the back of the hand.

In the case of sputum it is very important to pick out for the purpose of examination the small *greyish-white points* of pus, avoiding the mucus and the ordinary yellowish-green purulent discharge from the bronchi, etc.

The best results are obtained with sputum and the like by placing a small quantity of the material to be examined between two slides, which are squeezed together and then slowly and steadily drawn apart. The smears thus produced are again brought together and again drawn apart, and the

process is repeated until the material is evenly spread. The films are then dried and fixed.

Blood-films are best prepared in the following manner: Two very carefully cleaned slides are taken, and on the one, which is held in a horizontal position in the left hand, a drop of blood is placed near its right

Fig. 1.—Preparation of blood-films.

extremity. The other slide, held in the right hand, is now brought down on the drop in such a way that the blood spreads across its lower end and lies between it and the horizontal slide, to which it is inclined at an angle of about 45°. The slide in the right hand is now *pushed* steadily along the horizontal slide and *draws* the blood after it so that a thin and even film is left upon the second slide (Fig. 1).

The film is allowed to dry in the air, and then fixed either in the process of staining with Leishman's or Jenner's stain, or by ether-alcohol (ether 1 part, absolute alcohol 2 parts), or by heating in air at 120° C. for half an hour in some suitable apparatus.

Wet films.—When a culture of bacteria is to be investigated it is frequently a great advantage to examine it in a wet condition, both with and without the presence of a stain, as well as in dried films. Indeed this procedure should never be omitted in examining any culture, as many bacteria lose to a great extent their most characteristic morphological appearances when dried and killed

The following is the method to be used. A clean slide is taken, and upon it, at a little distance from each end, are placed two tiny drops, one of water, the other of dilute Czaplewski's fuchsin.[1] A little of the culture is rubbed up in each drop and a cover-glass placed upon each, care being taken to include some tiny air-bubbles to facilitate focusing. The drops must be so small that the cover-glasses *do not float* upon them, and that no fluid escapes around their edges.

If the *B diphtheriæ* is suspected, a wet film may also be put up with Bie's stain,[2] which very greatly facilitates the diagnosis. (*See* p 94, under *B. diphtheriæ*.)

Staining of dried films.—Dried films prepared as already directed may be stained by one of the following staining methods. In all cases damar dissolved in xylol is recommended for permanent mounting in preference to the use of Canada balsam.

SIMPLE STAINING WITH BASIC ANILINE DYES

1. Dry the film thoroughly in air.

[illegible] water

glacial

2. Fix by flaming, or (e.g. blood-films) in *ether-alcohol*.[1]
3. Stain with Czaplewski fuchsin,[2] neutral red,[3] thionin,[4] or methylene-blue,[5] for 2 minutes.
4. Wash with tap-water.
5. Dry roughly by pressing out beneath several thicknesses of filter-paper.
6. Dry *thoroughly in air.*
7. Mount in xylol damar.

ZIEHL-NEELSEN'S STAIN FOR ACID-FAST BACTERIA (TUBERCLE, ETC.)

1. Dry the film thoroughly in air.
2. Fix by flaming.
3. Pour on carbol-fuchsin[6] and heat till steam rises; then leave to stand for 5 minutes.
4. Wash rapidly with tap-water.
5. Decolorize with 25 per cent. H_2SO_4 for 3 to 5 seconds.
6. Wash with 60 per cent. alcohol till no more colour comes out.

Or, 5A. Decolorize with alcoholic aniline hydrochloride[7] till no more colour comes out

6A. Wash with tap-water.

Counterstain.

(*a*) Stain with malachite-green[8] or methylene-blue, for from ½ minute to 1 minute.

(*b*) Wash well with tap-water.

7. Dry roughly by pressing out beneath several thicknesses of filter-*paper.*
8. Dry thoroughly in air.
9. Mount in xylol damar.

GRAM'S STAIN

1. Dry the film thoroughly in air.
2. Fix by flaming, or *by ether-alcohol for 15 minutes.*
3. Stain with aniline gentian-violet, carbol gentian-violet,[9] or methyl-violet,[10] for 1 minute.
4. Pour off the stain.
5. Wash with solution of iodine in potassium iodide.[11]
6. Leave this solution on the film for 2 minutes.
7. Decolorize with absolute alcohol till no more colour comes out.

[1] Ether 1 part, absolute alcohol 2 parts.
[2] *See foot-note* (¹), p. 41.
[3] 1 per cent. watery solution of neutral red, with 5 per cent. of a 1 per cent.

carbolic acid add 10 c.c. saturated

blue.

[6] Basic fuchsin 1 grm, absolute alcohol 10 c.c. Dissolve, and add 5 per cent aqueous carbolic acid 100 c.c.
[7] 1 per cent. aniline hydrochloride in absolute alcohol.
[8] 1 per cent. watery solution of malachite green.
[9] *Carbol gentian-violet.* To 100 c.c. of ½ per cent. carbolic acid solution add 10 c.c. saturated alcoholic solution of gentian-violet. Allow to stand till next *day; filter.*
[10] 1 per cent. watery solution of methyl-violet.
[11] Iodine 1 grm., potassium iodide 2 grm, distilled water 300 c.c.

Counterstain.

(a) Wash quickly with tap-water.
(b) Stain with neutral red for from 1 to 2 minutes, or, for blood preparations, with eosin[1] for 2 minutes
(c) Wash with tap-water.

8. Dry roughly by pressing out beneath several thicknesses of filter-paper.
9. Dry thoroughly in air.
10. Mount in xylol damar.

Claudius's Stain

1. Dry the film thoroughly in air.
2. Fix by flaming, or, with e.g. blood-films, in ether-alcohol.
3. Stain with methyl-violet for 1 minute.
4. Wash with tap-water.
5. Treat with half-saturated watery picric-acid solution for 2 minutes.
6. Dry roughly by pressing out between several thicknesses of filter-paper.
7. Decolorize with picric-acid aniline oil[2] till no more stain comes out.
8. Wash well with tap-water.

Counterstain.

(a) Stain with neutral red for from 1 to 2 minutes.
(b) Wash with tap-water.

9. Dry roughly by pressing out between several thicknesses of filter-paper.
10. Dry roughly in air.
11. Mount in xylol damar.

Romanowsky's Stain (Giemsa's Solution[3]) for the Spironema pallidum, etc.

1. Dry the film thoroughly in air
2. Fix in ether-alcohol or absolute alcohol for 15 minutes.
3. Dry in air.
4. Wash with distilled water.
5. Stain for 15 minutes with freshly made stain (1 c c. of stain to 10 c.c. of distilled water), 60 minutes for the *Spironema pallidum.*
6. Dry roughly by pressing out beneath several thicknesses of filter-paper.
7. Dry thoroughly in air without heating
8. Mount in xylol damar.

Leishman's Stain

The stain is prepared by rubbing up 0 15 grm. of the dry powder[4] in a mortar, adding gradually methyl-alcohol (Merck's pure) to a volume of 100 c c.

[1] 1 per cent. watery solution of eosin.
[2] Aniline oil with a small quantity of picric acid added.
[3] This may be purchased from Grübler, Leipsic.
[4] The dry stain, which is a methylene-blue-eosin compound, can be obtained commercially.

1. Dry the film thoroughly in air.
2. Pour stain on to the *unfixed film, and leave for ½–1 minute.*
3. Add an equal volume of distilled water, mix by tilting the slide to and fro, and leave for from 5 to 10 minutes.
4. Wash with distilled water for 2 minutes.
5. Dry in air without heating.
6. Mount in xylol damar.

Staining spores.—The following method may be used *for staining* spores:—

1. Dry the film thoroughly in air.
2. Fix by flaming.
3. Pour on carbol-fuchsin, heat till steam rises, then leave to stand for 5 minutes.
4. Decolorize slightly with 1 per cent. sulphuric acid, or 1 per cent. hydrochloric acid.
5. Wash with tap-water.

   Counterstain.

   (*a*) *Stain with malachite green or methyl-green for ½ minute.*
   (*b*) Wash well with tap-water.
6. Dry roughly by pressing out between several thicknesses of filter-paper.
7. Dry thoroughly in air.
8. Mount in xylol damar.

Staining flagella.—This is a difficult and often uncertain process. The slides must be scrupulously clean, and quite young agar-cultures should be used (not more than 15 hours old). A small amount of growth must be taken on a platinum needle and carefully washed out into a few drops of distilled water in a watch-glass, avoiding violent movements of the needle or rubbing on the glass as the flagella are very easily broken off from the bacteria. A small drop of the emulsion, which must not exhibit more than a very faint turbidity, is placed upon a slide and gently stroked along its surface. It is then air-dried, and may be stained by either of the following methods:—

MUIR'S MODIFICATION OF PITFIELD'S METHOD

The *mordant* used is made up as follows:—

10 per cent. aqueous solution of tannic acid, 10 parts.
Saturated aqueous solution of corrosive sublimate, 5 parts.
Saturated aqueous solution of potash alum, 5 parts.
Carbol-fuchsin (Ziehl-Neelsen), 5 parts.

It must be freshly centrifugalized each time before use.

The *stain* is—

Saturated aqueous solution of potash alum, 25 parts.
Saturated alcoholic solution of gentian violet, 5 parts.

1. Prepare and fix the film as above directed.
2. Pour on the *mordant,* and heat over a flame until steam rises. Allow the fluid to steam for about 2 minutes
3. Wash *thoroughly in water.*
4. Dry completely in air.
5. Pour on the stain, and heat to steaming over a flame for about 2 minutes.
6. Wash thoroughly in water.

7. Dry in air.
8. Mount in xylol damar.

PLIMMER'S METHOD

The stain, which is not easy to prepare, can *be obtained ready-made*.[1]

1. A clean slide is heated and allowed to cool *to blood temperature*. A drop of the bacterial emulsion is placed at one *end, and allowed* to run down the slide, so as to dry quickly.
2. The stain, diluted 1 to 4 with water in a small tube, *is left to stand* for 1 minute, and then filtered on to the *unfixed film*.
3. Leave for 1 minute.
4. Wash quickly with tap-water.
5. Stain with carbol-fuchsin for 5 minutes.
6. Wash in tap-water.
7. Dry in air.
8. Mount in xylol damar.

Or, 1. Prepare and fix the film as above directed.
2. Pour on the *mordant*, and heat over a flame until steam rises. Allow the fluid to steam for about 2 minutes.
3. Wash thoroughly in water.
4. Dry completely in air.
5. Pour on the stain, and heat to steaming over a flame *for about* 2 minutes.
6. Wash thoroughly in water.
7. Dry in air.
8. Mount in xylol damar.

Staining capsules.—Capsules may be stained *by* [illegible] *method. The film must be very thin*

1. Dry the film thoroughly in air.
2. Stain with carbol-fuchsin for half a minute, *gently heating the slide* till steam begins to rise.
3. Wash quickly with methylated spirit.
4. Wash thoroughly with water.
5. Pour on the following *mordant* and leave *for 3 or 4 minutes*:
   Saturated solution of corrosive sublimate, 2 parts
   Tannic acid 20 per cent. solution, 2 parts,
   Potash alum in saturated solution, 5 parts
6. Wash thoroughly with water.
7. [illegible]
8. [illegible]
9. [illegible]
10. Wash, dehydrate in alcohol, clear in xylol, and mount in xylol damar.

Staining of sections.—Sections of tissues [illegible] may be stained for bacteria by the following methods:—

SIMPLE STAINING WITH BASIC ANILINE DYES

1. Treat with xylol for 1 minute.
2. Wash with xylol.

[1] From Mr. G. T. Gurr, 121, New King's Road, Fulham, S.W.

3. Remove xylol with absolute alcohol.
4. Stain with thionin, neutral red, or methylene-blue.
5. Wash with tap-water.
6. Treat with 1-per-cent. *acetic acid for 3 seconds.*
7. Dehydrate with absolute alcohol.
8. Clear with xylol.
9. Mount in xylol damar.

CARMINE-GRAM

1. Treat with xylol for 1 minute.
2. Wash with xylol.
3. Remove xylol with absolute alcohol.
4. Stain with lithium carmine [1] for 5 minutes.
5. Treat with picric-acid-hydrochloric-acid-alcohol [2] for 2 seconds.
6. Wash with tap-water.
7. Stain with aniline gentian-violet, carbol gentian-violet, or methyl-*violet for 2 minutes.*
8. Pour off the stain.
9. Wash with a solution of iodine in potassium iodide.[3]
10. Treat with a solution of iodine in potassium iodide for 3 minutes.
11. Decolorize and dehydrate with absolute alcohol until the carmine red again shows distinctly.
12. Clear with xylol.
13. Mount in xylol damar.

CARMINE-CLAUDIUS

1. *Treat with xylol for 1 minute.*
2. Wash with xylol.
3. Remove xylol with absolute alcohol.
4. Stain with lithium carmine for 5 minutes
5. Treat with 1-per-cent. HCl-alcohol for 5 minutes.
6. Wash with tap-water.
7. Stain with methyl-violet for 2 minutes.
 Wash quickly with tap-water.
9. Treat with half-saturated watery picric-acid solution for 3 minutes.
10. Pour off the above solution
11. Dry roughly by pressing out between several thicknesses of filter-paper.
12. Decolorize and dehydrate with picric-acid aniline oil until the carmine red again shows distinctly.
13. Wash off and clear with xylol.
14. Mount in xylol damar.

ZIEHL-NEELSEN

1. Treat with xylol for 1 minute.
2. Wash with xylol.
3. Remove xylol with absolute alcohol.
4. Stain with carbol-fuchsin, heating the slide gently, and *leaving for* 5 minutes.

[1] Carmine 5 grm., saturated solution of lithium carbonate in distilled water 200 c.c. *Boil and filter.*

[2] HCl-alcohol with a little picric acid added.

[3] "Lugol's iodine": iodine 1 grm, potassium iodide 2 grm., distilled water 300 c.c.

5. Wash with tap-water.
6. Decolorize with 25 per cent. H_2SO_4 for from 3 to 10 seconds.
7. Wash with 60 per cent. alcohol till only a faintly rosy colour remains.
Or, 6A. Decolorize with alcoholic aniline hydrochloride till only a faintly rosy colour remains.
7A. Wash with tap-water.
8. Stain with malachite green or methylene blue for 1 minute.
9. Wash with tap-water.
10. Dehydrate with absolute alcohol.
11. Clear with xylol.
12. Mount in xylol damar.

AGGLUTINATION REACTION

[illegible]

It may be observed either under the microscope or by the naked eye. In the former case, in which it is usual to make use of living bacteria, it is seen in the case of motile bacteria that shortly after the addition of agglutinating serum the movements of the micro-organisms become less active. They begin to adhere to one another, while those that remain free become increasingly sluggish in their movement. The clumps enlarge by fusion when they come into contact, as well as by the adhesion of still separate individuals, until in a complete agglutination practically all the bacteria are united into larger or smaller clumps. With non-motile organisms the events are similar, save that there is no motility to be affected.

If, on the other hand, the phenomenon is observed by the naked eye in a suspension to which agglutinating serum has been added in a small tube, the occurrence of the changes just described leads to a striking alteration in the appearance of the suspension. This consists in a gradual change from uniform turbidity [illegible] which steadily increases, and terminate[illegible]een added in sufficient strength, in th[illegible] the bacterial clumps.

The reaction as used clinically for the diagnosis of typhoid infection [illegible] Widal reaction [illegible]

it must be clearly stated that the only way in which constant, reliable, and satisfactory quantitative results can be obtained is by the *macroscopic* method of examination. In cases where any form of preventive inoculation against a particular infection has previously been administered, a trustworthy con- [illegible]

opacity and sensitiveness are required.

The method of carrying out agglutination tests and interpreting the results obtained will now be described.

Macroscopic method.—The test is carried out by Dreyer's method with standard cultures [1] in the following manner:—

Take a stand[2] (or stands) made to hold the special *agglutination tubes*, and place in it as many rows of five tubes as may be required and a dilution tube.

With the proper dropping pipette *held vertically*, measure out into the *dilution* tube as many times 18 drops of normal saline solution (0 85 per cent. sodium chloride in distilled water), as there are standard cultures to be used in the test. Thus, if three cultures are to be employed, measure out 54 drops of saline (where the water supply is pure, tap-water may be substituted for the saline solution).

Wash out the pipette with water.

Dry out the pipette with successive quantities of absolute alcohol, followed *by successive quantities of ether, and drive off the ether completely (or dry* the pipette with acetone).

Take up the serum to be tested into the pipette Measure out into the dilution tube containing the saline as many times 2 drops of the serum as *there are standard cultures to be tested. A dilution of* $\frac{1}{10}$ *is thus obtained.* Mix thoroughly.

Carefully wash out the pipette.

With the pipette measure out into each row of tubes as follows:

Number of tube	Drops of normal saline solution	Drops of serum dilution 1 in 10		
1	0	10	To each tube in row 1 add 15 drops of one of the standard cultures.	If a mark be made on the pipette corresponding to a volume of 15 drops, the fluid may be added without drop-counting.
2	5	5	To each tube in row 2 add 15 drops of another standard culture, if more than one is being used in the test.	
3	8	2		
4	9	1		
5	10	0	And so on, according to the number of cultures to be employed	

At each stage of the procedure the pipette is carefully washed with dis-
... absolute alcohol
...s suffice washed
...d. One and
the same pipette must be used throughout the operation.

Shake each tube thoroughly in order from right to left, i.e. beginning each row with the control tube.

Place the stand in a water-bath at 50°–55° C. (*not in dry air*), and leave it for 2 hours if the standard cultures used are *B. typhosus*, *B. paratyphosus-A*, *B. paratyphosus-B*, *B. enteritidis* (Gaertner), *B. coli*, or *Vib. choleræ*. Leave for 4½ hours if cultures of *B. dysenteriæ* (Shiga or Flexner) are in question.

[1] Standard cultures can be obtained by application to the Standards Laboratory (Medical Research Council), Department of Pathology, University of Oxford. Directions for their preparation can also be obtained

[2] Stands, dropping pipettes, agglutination tubes, etc., can be obtained from Messrs. Baird & Tatlock, 14, Cross Street, E.C.1, or from Messrs. R. B. Turner & Co., Eagle Street, W.C.1.

It is advisable to arrange the level of the water in the bath so that not more than the lower half to two-thirds of the columns of fluid in the tubes is immersed. Flocculation is thus accelerated, which is of the greatest importance in the case of dysentery tests.

In tube 1 of each row the serum acts in a dilution of 1 in 25.
„ 2 „ „ „ „ 1 in 50.
„ 3 „ „ „ „ 1 in 125.
„ 4 „ „ „ „ 1 in 250.

Tube 5 containing no serum is control against spontaneous agglutination.

If the limit of agglutination is not reached within this series, higher dilutions are followed out in a similar manner.

Thus, for example, 57 drops of normal saline solution plus 3 drops of

by a 15-to-20-minutes standing at room temperature. The reading is taken by comparing each tube in succession with the control tube, and should

It is always advisable to re-examine the tubes after a further period of 16 to 20 hours at room temperature, when possible zones of inhibition will have ceased to complicate the readings. The readings will be found to have moved on slightly in the interval.

ployed, it will commonly happen that no tube in the series exhibits *standard*

tination tubes are issued from the Standards Laboratory. These are prepared to show the precise degree of flocculation known as "standard agglutination," and are n
to the different cha
and the dysentery g
are required for the two groups.

Should a more precise determination of the limits of agglutination be

at room temperature with *B. typhosus*, *B. paratyphosus*, and similar bacilli. When this is done, 16 to 24 hours must be allowed before the reading is taken, but the reaction is not then so sharply defined. In this case the highest dilution in which a definite sedimentation with clearing of the

supern [illegible] dard agglutination.

[illegible] temperatures.

Wi [illegible] *agglutination*) occurs with standard agglutinable culture in a serum dilution of 1 in x, then x divided by the figure ("reduction factor") given on the label of the standard agglutinable culture employed gives the number of *standard agglutinin units* [1] contained in 1 c.c. of the serum examined.

Thus, if standard agglutination occurs in a dilution of 1 in 100 and the number on the label is 2, then $\frac{100}{2}$, i.e. 50, *is the number of standard agglutinin units contained in 1 c.c. of the serum examined.*

For uniformity *and simplicity in recording results* they should be expressed in *standard agglutinin units.*

I. *Diagnosis of Typhoid and Paratyphoid Fevers*

A. **In non-inoculated persons** who have *not* had typhoid (or paratyphoid) fever, agglutination in a dilution of 1 in 25 justifies a strong suspicion of typhoid (or paratyphoid) infection. But the test must be applied again in the course of a few days, to ascertain whether *there is any change in the titre of agglutination.* Marked agglutination in a dilution of 1 in 50 or more is (nearly always) diagnostic of active typhoid (or paratyphoid) infection.

A *non-inoculated* "carrier" will normally show no important change in the titre of his serum on repeated examination at short intervals

B. **Inoculated persons,** if quite recently inoculated with typhoid vaccine, will usually show a high titre of specific agglutination. A rapid rise in titre sets in within two to four days of inoculation. This is followed by a fall, at first rapid, but subsequently becoming very slow, so that a relatively high titre is maintained for a long period (even for years). During this period examinations made at intervals of a few days give practically identical readings

It follows that in the case of inoculated persons the diagnosis of active typhoid (or paratyphoid) infection will require two or more successive examinations of the serum.

(*a*) If [illegible] his titre of ty [illegible] sequent regular fall seen in non-inoculated [illegible] om and returning towards the higher base-line of inoculated persons.

(*b*) If the individual is suffering from active *paratyphoid* infection, one of three things may occur as regards his *typhoid* agglutination titre, namely:

1. No appreciable change may occur in the titre of typhoid agglutination.
2. A relatively slight rise may occur, followed by a fall towards the former level.
3. A marked rise may occur synchronous with the rise in paratyphoid agglutination titre, and subsequently followed by the usual fall towards the former level.

[1] [illegible] *agglutinin unit* was chosen as that amount of agglutinating [illegible] olume with normal saline solution causes [illegible] d with 1·5 *c.c. of a* particular standard [illegible] 55° C. for the exact period prescribed for [illegible] ours or 4½ hours—*see* p. 49), followed by [illegible] ure.

Meanwhile the titre of *paratyphoid* agglutination runs the normal course of rapid rise to a maximum (usually exceeding the maximum typhoid titre) followed by a fall, at first rapid and then slower as already described for typhoid subjects, and falling *below* the persistent base-line of typhoid agglutination of inoculated persons [1]

C. In the case of mixed infections, whether in inoculated or non-inoculated persons, the agglutinin curves for the different infecting organisms are usually not synchronous, and they pursue their ordinary course independently of each other.

II. *Diagnosis of Bacillary Dysentery caused by B. Shiga or B. Flexner (V, W, X, Y, and Z), by means of Standard Agglutinable Cultures*

A. In persons who do not give a history of bacillary dysentery and who have not been inoculated against dysentery, the presence of 10 [2] or more standard agglutinin units per cubic centimetre of serum is for all practical purposes diagnostic of an active bacillary dysenteric infection caused by the bacillus agglutinated. The presence of from 6 to 8 [2] units justifies a strong suspicion of dysenteric infection. In the [illegible]

before a diagnosis can be made, be necessary to carry out a second examination. If such a second examination, conducted 4 or 5 days after the first, shows a definite change (rise or fall) in agglutination titre, we are dealing with an active infection. But if no important change in the agglutination titre is shown the agglutination is to be attributed to a past infection.

C. A "carrier" in whom the infection is inactive will usually show no important change in his agglutination titre on repeated examinations at short intervals.

III. *Diagnosis of Bacillary Dysentery in Cases of Mixed Infection by Two or more Varieties of B. dysenteriæ*

When in the course of a differential diagnosis it is found that the patient

found that the rise and fall in agglutination to the different microbes will be synchronous. It is to be noted in connexion with co-agglutination that it is more common to see a co-agglutination of *B. Flexner* in a *B. Shiga* infection than of *B Shiga* in a *B. Flexner* infection.

When the case is one of mixed infection the agglutinin curves for the different infecting organisms are usually not synchronous, and they pursue their ordinary course independently of each other.

[1] For the diagnosis in persons inoculated with "triple" vaccine (typhoid, paratyphoid A, and paratyphoid B), *see* the *Lancet*, November 25, 1916, and March 10, 1917.

[2] In the case of *women* the figures 10 units and 6 to 8 units should be replaced by 20 and 12 to 16 respectively, for the serum of normal women exhibits a higher agglutination titre than that of normal men.

Microscopic method.—Serum is separated from the blood to be examined, and a number of dilutions (1 : 5, 1 : 10, 1 : 20, 1 : 50, etc.) are made with culture bouillon. This should by preference be done accurately with a graduated capillary pipette, but is sometimes done by placing a loopful of serum on a slide with a platinum loop, placing round it in succession as many loopfuls of bouillon as are needed for the dilution desired, and then mixing all the loopfuls together.

A young bouillon culture of the organism to be tested is then taken in hand (preferably not more than 18 hours old), and a measured quantity of this (or a loopful) is mixed with an equal measured quantity (or loopful) of diluted serum. From the mixture a hanging-drop is made, or a drop placed on a slide and simply covered with a cover-glass.

The effect of the serum is watched under the microscope. It is important that the culture be examined also without the addition of serum, to avoid the fallacy of spontaneous agglutination of the bacteria; and for the same reason emulsions from agar should, preferably, not be used.

As regards the diagnosis of enteric fever, it is usually agreed that a positive reaction within 20 minutes, with a total dilution of the serum of 1 in 50, justifies a diagnosis of typhoid infection.

Determination of the Opsonic Index

In this determination the serum of the patient is compared with the serum of a healthy individual, or, better, with a "pooled" serum from a number of healthy persons, in respect of its power of "preparing" the bacteria in a given bacterial emulsion for phagocytosis by normal washed leucocytes.

1. **Preparation of normal leucocytes.**—About ½ c.c. of blood is taken from the observer's finger into about 3 c.c. of a 1.5-per-cent. solution of sodium citrate in 0.85-per-cent. sodium chloride solution, the tube being gently shaken as the blood drops into it, to ensure thorough mixing and prevent coagulation. The mixture is then centrifugalized, and the supernatant fluid removed and replaced by normal salt solution. The blood-corpuscles are then shaken [illegible]
fully remove[illegible]
number of th[illegible]
for use.

2. **Preparation of serums.**—Blood is taken into a Wright's blood capsule or other suitable small tube to the amount of about ½ c.c. It is allowed to clot, and the vessel is then placed in a centrifuge, and the serum thus separated. The operation is performed with blood from the patient, and with blood from the control individual (or group of individuals). The serums thus obtained should be used as quickly as possible, that is to say, while they are still quite fresh.

3. **Preparation of bacterial suspension.**—In the case of rapidly growing micro-organisms a little of a 24-hour-old sloped-agar surface culture is taken and rubbed up in a few drops of 0.85-per-cent. saline solution, the resulting emulsion is added to several c.c. of saline solution in a tube and centrifugalized to get rid of any unbroken masses or clumps of undissociated bacteria. The fluid suspension is pipetted off, and diluted

until it shows only a very faint turbidity, when, according to Wright, it will contain the most appropriate number of bacteria.

In the case of organisms which grow only on special media, or grow very slowly, suitable cultures must be used for preparing the bacterial suspension. In the case of the *B. tuberculosis* it is probably most convenient for those who are not expert bacteriologists to purchase one of the preparations stocked commercially, and make up from this a suspension of the proper strength in 1·5 per-cent. saline solution. The test is carried out in the following way: A piece of glass tubing is drawn out at one end into a capillary tube, and the other end is provided with a rubber nipple. A mark is made on the capillary about an inch from its lower end, and to this mark serum is drawn up, a small air-bubble is admitted, and the bacterial suspension is drawn up to the same mark. The two portions of fluid are then blown out upon a clean slide, sucked up again, and again blown out several times to ensure complete mixing. The mixture is now drawn up into the tube, a small air-bubble admitted, and leucocyte suspension (which has been previously well mixed by gentle shaking) is taken in up to the mark. The whole is blown out upon the slide and mixed as before. The fluid is finally taken up into the pipette, a little air admitted, and the end of the capillary sealed up in a small flame. Two pipettes are thus prepared, the one with normal serum and the other with the serum under investigation. The pipettes are incubated at 37° C. for a quarter of an hour, are then opened at the point, the contents of each are again well mixed, and films prepared. These are either fixed in corrosive-sublimate solution for a few seconds and then well washed and stained appropriately (in the case of *B. tuberculosis* the Ziehl-Neelsen method is used), or fixed and stained by using Leishman's stain.

In each film the number of bacteria in not less than 100 leucocytes (preferably 200) is counted, and the average number per leucocyte thus arrived at. The *ratio* which this average in the case of the patient bears to the average in the control prepared with normal serum is called the *opsonic index* of the patient's serum.

SERO-DIAGNOSIS OF SYPHILIS

I. Wassermann Reaction

The technique recommended is in all essentials that described by Fildes and McIntosh in Report No. 14 of the Medical Research Council, 1918, where the full details are given.

A. *Reagents and Apparatus required*

1. *Serum to be tested.*—Some 2-5 c.c. of blood is drawn aseptically from a superficial vein and placed in a sterile tube. The serum is taken off the clot and heated to 55°–56° C. for 30 minutes. It is essential that the syringe or needle used for drawing the blood should contain neither alcohol, ether, nor other disinfectant.

2. *Antigen.*—This consists of a 1-in-15 saline suspension of a mixture of alcoholic extract of human heart-muscle and an alcoholic cholesterin solution in the proportion of 3 : 2. The dose of antigen is 0·5 c.c. of this suspension. The alcoholic heart-extract is made by grinding up 10 grm. of human heart-muscle with 90 c.c. of absolute alcohol. Put into a glass-

stoppered bottle for 1½ hours and shake occasionally. Filter into a glass-stoppered bottle and preserve in ice-chest.

The alcoholic cholesterin solution is made by dissolving 1 grm. of pure cholesterin in 100 c.c. of absolute alcohol, warming until dissolved. Keep in a glass-stoppered bottle.

3. *Complement.*—Fresh guinea-pig's serum is used. The blood having been collected and left to clot, the serum is pipetted off.

4. *Amboceptor*.—This can either be bought or made by repeated intraperitoneal injection into a rabbit of washed red blood-corpuscles of sheep. The animal is bled about the eighth day after the last injection, the blood allowed to clot, the serum separated, distributed in small sterile phials, and heated to 56° C. for 30 minutes to remove complement. Store in an ice-chest.

5. *Red cells.*—Sheep's blood is whipped to prevent clotting, the serum centrifugalized off, and the red cells are washed three times with saline. A 5-per-cent. suspension of these cells in normal saline is used for the test.

6. *Normal saline*, made by dissolving 9 grm. of sodium chloride in 1 litre of freshly distilled water and autoclaving.

7. 1-c.c. and 10-c.c. *pipettes*, graduated to tip.

8. *Dwarf test-tubes*, 7 cm. by 1 cm.; *ordinary test-tubes.*—Tubes should be cleaned by soaking in acid, then rinsed with ordinary water and finally with distilled water, and dried in the oven.

9. *Racks* to hold dwarf test-tubes.

10. *Water-baths*, one to be kept at 37° C. for carrying out the test, the other at 55°–56° C. for heating the serum to be tested.

B. *Carrying out the Test*

Two preliminary tests have to be carried out—the first to determine the minimal hæmolytic dose (M.H.D.) of the amboceptor in the presence of 0·1 c.c. of a 1 : 2 dilution of complement; the second to determine the minimal hæmolytic dose (*M.H.D.*) of the complement.

The *first* test is carried out in the following manner and with the following quantities:—

No. of test-tube	*Saline*	*Amboceptor*. 1 : 1,000 dilution in saline	*Complement*: 1 : 2 dilution in saline	*Red cells*: 5-per-cent. suspension in saline
1	0 c.c.	0·9 c.c.	0·1 c.c.	0·5 c.c.
2	0·1 ,,	0·8 ,,	0·1 ,,	0·5 ,,
3	0·2 ,,	0·7 ,,	0·1 ,,	0·5 ,,
4	0·3 ,,	0·6 ,,	0·1 ,,	0·5 ,,
5	0·4 ,,	0·5 ,,	0·1 ,,	0·5 ,,
6	0·5 ,,	0·4 ,,	0·1 ,,	0·5 ,,
7	0·6 ,,	0·3 ,,	0·1 ,,	0·5 ,,
8	0·7 ,,	0·2 ,,	0·1 ,,	0·5 ,,
9	0·8 ,,	0·1 ,,	0·1 ,,	0·5 ,,

Shake the tubes and incubate in the water-bath for 1 hour at 37° C. Then read off the minimal hæmolytic dose of amboceptor, i.e. the last tube showing complete hæmolysis. *If none of the tubes shows complete hæmolysis, the*

amboceptor should be rejected. This test of amboceptor should be repeated every two months, as the amboceptor is liable to deteriorate in time.

The *second* test is carried out in the following manner and with the following quantities, and *must be made each time the reaction is put up* :—

No. of test-tube	*Saline*	*Complement : 1 : 25 dilution in saline*	*Antigen : 1 : 15 suspension in saline*	*Sensitized red cells*
1	0 7 c.c.	0 3 c.c.	0 c c.	0 5 c.c.
2	0 75 ,,	0 25 ,,	0 ,,	0 5 ,,
3	0 8 ,,	0 2 ,,	0 ,,	0 5 ,,
4	0 85 ,,	0 15 ,,	0 ,,	0 5 ,,
		Complement : 1 : 10 dilution in saline		
5	0 2 ,,	0 3 c.c.	0 5 ,,	0 ,,
6	0 25 ,,	0 25 ,,	0 5 ,,	0 ,,
7	0 3 ,,	0 2 ,,	0 5 ,,	0 ,,
8	0 35 ,,	0 15 ,,	0 5 ,,	0 ,,

Place in the water-bath at 37° C for 10 minutes. If tube 1 is not completely laked by this time, the complement is not strong enough, *and should be discarded.* If laked, continue incubation for 50 minutes more, read M.H.D. of complement in tubes 1 to 4, and add 0 5 c c. of sensitized red cells to tubes 5 to 8. Place in water-bath for 10 minutes and then read. If, for example, tubes 3 and 7 are completely laked, and tubes 4 and 8 are not, 0 2 c.c. of a 1 : 25 dilution of complement is the M.H.D. of the complement. But if tube 7 is not completely laked, and tube 6 is, 0 25 is the M.H.D. If tube 6 is not completely laked, the complement is unsuitable.

The sensitized red cells referred to are prepared by adding 4 M.H D. of amboceptor to 0 5 c.c. of a 5-per-cent suspension of red cells. If, for example, a total of 50 0 c c. of sensitized red cells is required, and the M H.D. of amboceptor is 0 5 c.c. of 1 : 1,000 dilution, the quantities required are 2·5 c.c. washed centrifugalized cells, 47 5 c c. saline, and $\frac{100 \times 4 \times 0\ 5}{1{,}000}$ = 0 2 c.c. undiluted amboceptor.

In the test proper 0 5 c c. of a dilution of complement should contain 2½ M.H.D. of complement. For example, if 0 2 c c. of a 1 : 25 dilution is the M.H.D., then 0 5 c.c. of a 1 : 25 dilution of complement contains 2½ M.H.D.

The final test is now put up as follows :—

No. of tube	*Serum to be tested, diluted 1 : x in saline*	*Saline*	*Antigen*	*Complement*
1	0 1 c.c. 1 : 1	0 c c.	0·5 c.c.	0·5 c.c.
2	0 1 ,, 1 : 2	0 ,,	0 5 ,,	0 5 ,,
3	0 1 ,, 1 : 4	0 ,,	0 5 ,,	0 5 ,,
4	0 1 ,, 1 : 8	0 ,,	0 5 ,,	0 5 ,,
5	0 1 ,, 1 : 16	0 ,,	0 5 ,,	0 5 ,,
6	0 1 ,, 1 : 1	0 5 ,,	0 ,,	0 5 ,,

Shake the tubes and incubate in the water-bath at 37° C. for 1 hour, then [illegible]

[illegible] chest over-night, and read the degree of hæmolysis next day. If tube 6 does not show complete hæmolysis, another specimen of the serum should be tested.

Readings and diagnosis.—The readings should be recorded in degrees of hæmolysis, where 4 = total hæmolysis, 3 = 75 per cent. hæmolysis, 2 = 50 per cent. hæmolysis, 1 = 25 per cent. hæmolysis, and 0 = absence of hæmolysis. Thus, a negative serum will be recorded as 4, 4, 4, 4, 4. A strong positive serum, for example, as 0, 0, 0, 1, 4. A doubtful serum as 2, 4, 4, 4, 4.

If a serum, then, gives 50 per cent. or more hæmolysis in the first tube, the result must be recorded as doubtful unless there is a definite history of syphilis, or actual signs are present.

When testing *cerebro-spinal fluids*, use twice as much cerebro-spinal fluid as serum, and do not heat to 55°–56° C.

II. Sigma Reaction (Dreyer-Ward)

This is a flocculation reaction (avoiding the use of a hæmolytic system) based on the principle of the Sachs-Georgi reaction, but differing from it in the following details: (1) It is more sensitive than the Sachs-Georgi reaction. (2) It is quantitative as well as qualitative. (3) The antigen used is stable, and the saline suspension of this antigen is made in a manner that secures identical suspensions on every occasion, thus allowing a comparison and standardization of different antigens. (4) Accordingly, the results can be expressed in a standard unit system, i.e. a positive serum is said to contain so many standard units per c c. (5) The standard unit is readily maintained and checked.

A. *Reagents and Apparatus required*

1. *Serum to be tested.*—Some 4 to 5 c.c. of blood are withdrawn from a superficial vein with the same precautions as already indicated for the Wassermann reaction. The serum is pipetted off into a sterile tube and heated in a water-bath to 55° C. for 90 minutes.

2. *Antigen.*—(*a*) An alcoholic extract of calf's heart-muscle is prepared in the manner described by Bordet and Ruelens (*Comptes-Rendus de la Soc. de Biol.*, 1919, vol. lxxxii., p. 880). This extract contains the acetone-insoluble, alcohol-soluble substances of the heart-muscle. It is limpid, yellow in colour, and remains unchanged for a very long period. (*b*) A 1-per-cent. alcohol solution of cholesterin prepared as for the Wassermann reaction. Both these solutions should be kept in glass-stoppered bottles in the dark. To make the suspensions in saline, mix 5 0 c.c. of (*a*) with 0 25 c.c. of (*b*). Measure 1·0 c.c. of this mixture into a clean dry 100-c.c. measuring cylinder, placing the pipette on the bottom of the cylinder before allowing the fluid to run out. Sterile normal saline is dropped on to the alcoholic mixture from a constant height (36 cm.) at a constant rate which will deliver 10·7 c.c. in 1 minute 25 seconds. The resulting suspension is known as suspension α. To make the second suspension—suspension β—the same amount of alcoholic mixture is used, but the saline is allowed to drop at the same rate for 4 min. 30 sec., thus delivering 34·0 c c. The respective

suspensions should be gently mixed, not shaken. (The [illegible] of the suspensions to flocculation by syphilitic serum depends greatly on the rate at which the saline is allowed to drop on to the [illegible]. The rate given above is chosen because it secures maximum [illegible] and at the same time the suspensions show no visible particles with a [illegible] magnification lens. If the rate is faster, the suspensions [illegible]; if slower, particles may be seen with the 6-magnification lens.

3. *Saline solution* is made by dissolving 9·0 grm. of pure [illegible] in a litre of freshly distilled water, and autoclaving.

4. A *dropping apparatus* to secure at all times the [illegible] rate of dropping is [illegible]

5. *Agglutination* [illegible] with those used fo[illegible]

6. The results [illegible] manner described for agglutination, or by using a special [illegible]. The latter is of advantage if the room cannot be darkened, or the [illegible] is inexperienced.[2]

7. A 6-magnification *lens.*

8. Two properly regulated *water-baths,* one to be kept at 37° C. [illegible] at a temperature of 55° C.

B. *Setting up the Test*

The test is carried out in the following manner and [illegible] quantities, using the dropping pipette:—

TABLE I.

No. of tube	*Drops of saline solution*	*Drops of serum*	*Drops of suspension*	[illegible]
1	0	20 1 : 1	0 (α [illegible]	
2	0	10 „	15 (β [illegible]	
3	5	5 „	15 „	
4	8	2 „	15 „	
5	9	1 „	15 „	
6	0	10 1 : 20	15 „	
7	5	5 „	15 „	
8	8	2 „	15 „	
9	9	1 „	15 „	

A control tube containing 20 drops of saline and 6 [illegible] and another control tube containing 10 drops of sa[illegible] β-suspension, should always be made up and placed [illegible] pipette must be *held vertically, and one and the same* [illegible]. It will be found *convenient* to use an ordinary [illegible], the pipette with distilled water, and drying it [illegible] each stage.

[illegible]

the first five tubes, the 1 : 20 dilution must be [illegible]

The tubes are removed from the water-bath [illegible]

[1] These and the dropping apparatus may be [illegible] Turner & Co., Eagle Street, W.C.1.

[2] This apparatus, and specially arranged [illegible] obtained from the Oxford Scientific Instrument [illegible] Street, Oxford.

hours, and read. In the case of negative or border-line serums (i e. serums *containing* 1·5 Σ units or less), the first three tubes are incubated for a further period of 20–22 hours, and again read.

It is important to arrange the level of the water in the bath so that not more than the lower half to two-thirds of the column of fluid in the tubes is immersed.

C. *Reading of Results*

The terms used in describing the different degrees of flocculation met with are those used in the agglutination technique, viz. *total* (t), *standard* (s), *trace* (tr), and *nil* (0).

Total flocculation (t) indicates a condition where the fluid in the tube has become nearly clear, with the bulk of the large flocculi settled down at the foot of the tube.

Standard flocculation (s) is the degree of flocculation that can readily be seen with the naked eye. The fine flocculi are evenly distributed, of uniform size, and definitely separated from one another. The fluid accordingly shows some degree of clarification

Trace (tr) is the term applied to a very fine flocculation, not visible with certainty to the naked eye by most persons, while readily visible with the 6-magnification lens.

Nil (0) indicates that no flocculation is recognizable by means of the [illegible]

6-magnification lens. The latter, lation that can only be detected on occasions it may be difficult, decide certainly whether floccula (tr ?) is then applied. Any tube showing less than *trace* should for safety be compared with the control tube showing no flocculation.

To secure uniformity in readings by various observers, tubes exhibiting two [illegible] standard and trace and a control tube without floccu- [illegible] issue A [illegible] is reading

D. *Expression of Results in Standard Units*

All readings should be expressed in terms of standard flocculation units. The number of standard flocculation units in a serum is arrived at in the following manner:—

The amount of serum which, when made up to 1 0 c.c. volume with normal [illegible] c.c. of a par- [illegible] ued to contain [illegible] measured by [illegible] expressed in [illegible] he dilution in [illegible] veness of the

[1] It is to avoid the expression of positive results in fractions of a single unit that four units are taken instead of one unit as the basis of this unit system.

TABLE III (20–22 HOURS INCUBATION)

Degree of flocculation	*Number of tube*								
	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*
t	1 60	3 20	6 7	16 8	33 9	59	118	298	592
t −	1·29	2 58	5 4	13 5	27 2	47 5	95	240	477
s +	1·01	2·02	4 2	10 6	21 3	37 2	74	187	373
s	0 80	1 60	3 3	8·4	16 9	29 5	59	149	296
s −	0 67	1 35	2 8	7·1	14 2	24 8	49 5	125	248
tr +	0 57	1 14	2 37	6 0	12 0	20 9	42	106	210
tr	0 48	0 96	2 00	5 0	10 2	17·7	35 4	89	178
tr −	0·42	0 83	1·73	4 4	8 8	15 3	30 7	77	154
tr ?	0 33	0 66	1 37	3 4	6 9	12 1	24 2	61	121

TABLE IV (40–44 HOURS INCUBATION)

Degree of flocculation	*Number of tube*		
	1	2	3
t	0 83	1 05	3 44
t −	0 70	1·40	2·92
s +	0 58	1 15	2·40
s	0 48	0 96	2 00
s −	0 42	0 85	1·76
tr +	0 37	0 75	1 56

is calculated from Tubes 8 and 9.

Serums which, after a 20–22 hours incubation, give more than 1 5 Σ units, as calculated from Table III, × suspension factor of heart-extract used, should not be incubated any further. In such cases the readings after an incubation of 20–22 hours are final.

factor of the heart-extract used.

The reason for this further incubation is that certain serums have a slow

E. *Interpretation of Results*

1. Serums which contain more than 1·5 Σ units per c.c. are to be considered positive.

2. Scrums which contain from 1·0 to 1·5 Σ units per c.c. are to be considered [illegible] and these low unit-values are of

3. [illegible]

not qualitative in character.
4. Cerebro-spinal fluids which contain more than 1·0 Σ unit per c c. are to be considered positive.
5. Cerebro-spinal fluids which contain less than 1 0 Σ unit per c c. are to be considered negative.

E. *Precautions to be observed*

1. If a serum is obviously infected it should be discarded.
2. No preservatives, such as phenol, formalin, etc , should be added to any of the reagents
3. All tubes, pipettes, saline, etc., must be scrupulously clean.

III. SPECIAL BACTERIA

1. COCCI

Staphylococcus pyogenes aureus (Plate 1, Figs. 1 and 2).—The connexion of micrococci which grew in clusters with many suppurative conditions had been studied by Koch, Pasteur, and Ogston, but it was Rosenbach who, in 1884, first clearly differentiated and named the various pyogenetic cocci commonly met with. Ogston had already demonstrated the close relationship of "cluster" cocci to wound-infection, to osteo-myelitis, and to localized suppurative conditions in general. The work of Becker, who obtained pure cultures, and the investigations of Rosenbach afforded definite proof of the pathogenetic action of the staphylococci, and especially the *Staphylococcus pyogenes aureus*

The micro-organism is a spherical or nearly spherical coccus with a diameter of about 0 7 μ to 0 9 μ, but it may exhibit very much greater variations in size under particular conditions of temperature, culture medium, etc The cocci are commonly arranged irregularly in larger or smaller groups, but may appear chiefly in pairs. Moreover a microscopic film will generally present numerous isolated individuals, short chains of three or four, and even tetrads. The staphylococci are non-flagellated and non-motile.

The organism stains readily with aqueous solutions of most basic aniline dyes, either in a wet preparation or in a dried film (cf. Technique, p. 41). It is also stained by certain acid dyes, such as eosin, and fairly well by hæmatoxylin. It is Gram-positive, as are all the staphylococci.

It is aerobic, and a facultative anaerobe. It grows well on all ordinary media at the room temperature, but much more luxuriantly

at the body temperature. Its optimum is about 30° C., and its range of growth from about 10° C. to about 40° C.

The cultures show a rich golden-coloured pigmentation, but only form their pigment in the presence of free oxygen.

In bouillon at 37° C. the organism rapidly produces a uniform turbidity. It occasionally *forms a thin film upon the surface*, and after a few days exhibits an abundant and somewhat slimy deposit at the foot of the tube.

In a gelatin-stab, growth occurs along the whole length of the stab, but most luxuriantly near the surface, where peptonization of the medium commences in the course of a few days, and leads to the formation of a *cone* of liquefaction. At the apex of the cone is found a golden-coloured mass of deposited growth.

On the surface of agar (at 37° C.) the growth appears as a moist and paint-like orange-coloured streak most deeply pigmented along the centre of the growth and paler at the edges. This is due to the fact that the development of colour increases as the culture becomes older, and is accordingly most marked in the oldest part of the growth.

On potato the organism grows well, and upon this medium the pigmentation is particularly well marked.

When grown in milk it causes coagulation within a day or two at 37° C.

In culture it is readily distinguished by its rich orange pigmentation, and is only likely to be confused in this respect with the *Sarcina aurantiaca*.

The staphylococcus aureus shows considerable resistance to unfavourable conditions. Some strains survive heating for an hour at 70° C. even in a moist condition, though many are killed in about half an hour at temperatures between 50° C. and 60° C. It is killed with certainty in half an hour at 80° C.

In cultures upon agar or gelatin it will live for a year or more, and when in a dry condition on indifferent material it may be found alive and virulent even after many months.

Against the more commonly used antiseptics it exhibits moderate resistance. A 3-per-cent. solution of carbolic acid kills the organism in a few minutes (5–10), while a 1-per-cent. formaldehyde solution requires about an hour to ensure sterility. Mercuric chloride, while *inhibiting* its growth in quite weak solution, is particularly *ineffective* as a destructive agent for the staphylococci, since in a strength of 1 : 1,000 it takes about 20 hours to kill these organisms in a drop of pus. The micro-organism is remarkably susceptible to the action of certain aniline dyes; thus, methyl-violet in a dilution of 1 : 25,000 will kill it in the course of 15 minutes; and a closely allied dye has been extensively used under the name of pyoktanin in ophthalmic surgery.

The organism produces powerful tryptic ferments, and in cultivation it can liquefy not only gelatin but frequently coagulated blood-serum also. This fact is of importance in relation to the destruction and disintegration of tissue which occur in conditions of local suppuration and abscess-formation.

In addition to these ferments there are often found in filtered bouillon cultures toxic substances exhibiting hæmolytic and leucotoxic (leucocyte-destroying) properties, as well as others which produce upon injection local areas of extensive cell necrosis, or when circulating in the blood occasion special changes in the kidneys, and may even lead to amyloid degeneration in a variety of organs.

When inoculated into animals, the living organism leads to the local formation of an abscess, and may produce a general infection *terminating in a condition of pyæmia* Such a *pyæmia usually exhibits* numerous secondary foci in the heart and kidneys, and is often accompanied by suppurative arthritis. Osteo-myelitis hardly ever occurs under such conditions unless a bone has previously been injured. The virulence of the organism is very rapidly increased by passage from animal to animal.

The human subject is even more susceptible to the pathogenetic action of staphylococci than are most animals. Even if the micro-organism be merely rubbed into the skin a series of boils or local abscesses may be produced. It is indeed the commonest causal agent of cutaneous inflammations, especially those which are associated with suppuration, and it is very frequently met with in acute osteo-myelitis, in acute abscesses in any situation, and in ulceration of the cardiac valves

This staphylococcus may give rise to general infection and lead to a condition of pyæmia, though fortunately this result is relatively uncommon considering the enormous frequency of local inflammatory processes in which this organism is the causal agent.

While the attempt to obtain a satisfactory antitoxin for the treatment of staphylococcal infection has at present yielded no results of practical value, the use of staphylococcus vaccine in local infection, and especially in cutaneous suppurations, appears in many cases to have been attended with remarkable success.

Staphylococcus pyogenes albus.—This organism is closely similar to the *Staphylococcus pyogenes aureus.* It is distinguishable from the latter neither by its biological characters, nor by its distribution, nor even by its pathogenetic action, but only by its lack of pigmentation, and possibly also at times by its failure to produce liquefaction of gelatin. On solid culture media it presents itself as an opaque white slimy growth.

Staphylococcus epidermidis albus (Welch). — This staphylococcus is commonly present on the human skin. It is only very *slightly* virulent, and liquefies gelatin either very slowly or not at all. It is believed to be the usual causal agent in producing small stitch abscesses. Not improbably it is merely an attenuated form of the ordinary white staphylococcus pyogenes.

Staphylococcus pyogenes citreus. — Indistinguishable from the variety aureus except by its lemon-yellow pigmentation. It is only seldom found, but a non-virulent saprophytic organism often met with—the *Micrococcus flavus*—may easily be mistaken for it. This organism is, however, distinguished from the staphylococcus citreus by the fact that it does not coagulate milk, and only liquefies gelatin very slowly.

Staphylococcus cereus albus and **Staphylococcus cereus flavus.**—These are much less common and less virulent than the other members of the group. They are distinguished by the wax-like growth which they produce, and by the fact that they *do not* liquefy gelatin. They may be met with along with other staphylococci in suppurative conditions, but they are probably only present in these cases as saprophytes.

Micrococcus tetragenus (Plate 1, Fig 3).—The *Micrococcus tetragenus* was discovered by Gaffky, and is distinguished by its habit of dividing in two planes at right angles to each other, thus giving rise to the appearance of groups of four, or tetrads. The organism possesses a definite capsule when found in the animal body, but loses it in artificial media. It is non-flagellated and non-motile. It is Gram-positive. By the counterstaining of a Gram-preparation with eosin the capsule can be well shown.

The organism grows aerobically on all ordinary media as a porcelain-white, shiny, tenacious film; it does not liquefy gelatin, and its growth in bouillon appears as a very slight turbidity near the surface with a copious and tenacious slimy deposit. The micro-organism is pathogenetic for small laboratory animals, and especially so for mice. It is doubtful whether it is ever in itself definitely pathogenetic for man, though cases of septicæmia due to this organism have been described in children. But it is frequently met with as a secondary infection in suppuration in and about the respiratory passages, especially in the lung cavities of phthisis.

Sarcina.—The term sarcina is applied to a large group of micrococci which are distinguished by their somewhat large size, and by their habit of multiplying by division in three directions mutually at right angles, thus giving rise to packets of eight cocci. They are non-motile and have no flagella. They stain well with ordinary basic aniline dyes. They are Gram-positive.



Fig 1.—Staphylococcus pyogenes aureus from pure culture Stained by Gram's method × 850



Fig 2.—Staphylococcus in section of kidney abscess. Stained by Gram's method. × 750.

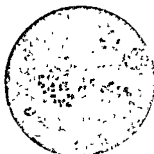


Fig 3.—Micrococcus tetragenus in section of kidney Stained by Gram's method. × 750

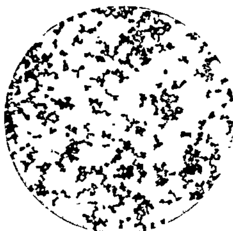


Fig. 4.—Sarcina aurantiaca from pure culture Stained by Gram's method × 850

PLATE 1.

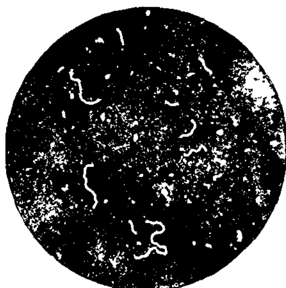


Fig. 1.—Streptococcus pyogenes from pure culture. Indian-ink method (Burri). × 1,000.

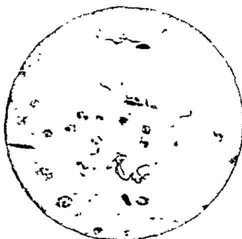


Fig. 2.—Streptococcus pyogenes in section of kidney. Stained by Gram's method. × 850

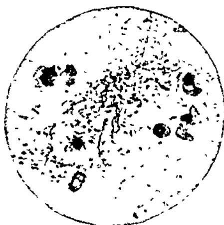


Fig. 3.—Pneumococcus in pus. Stained by *Gram's method* × 750.

PLATE 2.

It is doubtful whether any of them are pathogenetic for man, though several varieties have been isolated from the human body, and named accordingly *S. ventriculi*, *S. pulmonum*, and so on.

Many of them are strikingly pigmented organisms, and different varieties exhibit white, yellow, orange, lemon, brown, red (a whole series), and violet coloration.

They grow very readily on all the ordinary media, presenting on an agar-slope a thick, raised, moist, and shiny, paint-like streak of the appropriate colour. Many of them liquefy gelatin rather freely, though a few possess no such peptonizing action. In bouillon they produce a very copious sediment, the fluid remaining in some cases clear, in others exhibiting a uniform turbidity.

They are only likely to be met with by the surgeon in stomach contents, in the air-passages, or in the fæces, and will readily be distinguished from pathogenetic forms by microscopical examination alone.

Besides the forms already mentioned, *S. lutea*, *S. aurantiaca* (Plate 1, Fig. 4), *S. flava*, *S. cervina*, and *S. fusca* may occasionally be found in the alimentary canal or the respiratory tract.

Streptococcus pyogenes (Plate 2, Figs. 1 and 2).—Koch and Ogston were the first to draw a clear distinction between the streptococci and the staphylococci. In this country the latter observer carried out a careful study of their connexion with suppurative conditions, and indeed laid the first foundations for the scientific study of the pyogenetic cocci. He showed that while the "cluster" cocci were more commonly associated with localized suppurations, the "chaplet" or chain cocci were usually associated with spreading inflammations and phlegmonous conditions. Pure cultures of streptococci were first obtained by Fehleisen and Rosenbach, who thus opened the way for the exact experimental investigation of their pathogenetic action.

The *Streptococcus pyogenes* is a rounded coccus about 1 μ in diameter, arranged in shorter or longer chains of from 3 or 4 to as many as 50 or more individuals. Along with the chains are numerous diplococci and, it may be, a number of isolated cocci. The longest chains are met with in cultures made in fluid media. A variety of the organism which in fluid media forms very long chains will, when cultivated upon solid media or when found growing in the body fluids, usually be observed to present only quite short ones. The organism is frequently somewhat flattened from side to side where it is in contact with its neighbours in the chain. It is non-motile and has no flagella. When growing in the animal body some strains of streptococci present a well-marked capsule (*S. mucosus*).

The streptococcus stains readily with all the ordinary basic aniline

dyes both in wet preparations and in dried films. It is Gram-positive (but easily decolorizable forms are sometimes found).

It is aerobic, and a facultative anaerobe. Its optimum temperature is about 37° C., and its limits of growth are from 12°–15° C. to about 42° C.

In bouillon at 37° C. the growth frequently appears in the form of tiny granules in a clear fluid, the granules falling to the bottom to form a fine deposit. In other cases small spherical masses of growth are formed (*S. conglomeratus*), or flocculi, and sometimes there is a more or less uniform turbidity. These differences depend in a great degree both on the length of the chains and on the extent to which these chains become coiled.

In a gelatin-stab (at 22° C.) growth takes place rather slowly, and the medium is not peptonized by the culture. Growth appears along the stab in the form of a series of small rounded colonies which afterwards become fused. Very little if any surface growth occurs. On the surface of agar there are formed a number of tiny, delicate-looking, greyish colonies, which are somewhat translucent. Even when few in number the colonies never reach any considerable size, and when they are numerous and thickly set they do not completely fuse. On potato, usually, no visible growth occurs.

In culture many minor variations appear, and some of them have been made use of in attempts to devise a definite classification of streptococci. On the whole it may be stated that the long-chained forms will be found to be more virulent than the shorter ones. The streptococci are delicate in culture, and unless transplanted will usually die out in from two or three days to about a fortnight. But if desiccated, as, for example, in dried pus and other discharges, they can survive and retain their virulence, at any rate for months. Some strains can resist a temperature of 60° C. for an hour or more, but they are killed by an exposure to 70° C. for the same period. A 3-per-cent. carbolic-acid solution kills the organism within a few minutes.

Different streptococci ferment solutions of various sugars in different degrees with a production of carbonic-acid gas. They also produce lactic acid, and several acids of the fatty-acid series (formic, acetic, etc.). Specific toxins have not been isolated from their cultures, but toxic albumoses, hæmolytic substances, and other poisonous bodies are found in bouillon cultures of the organism.

The fermentation tests introduced by Gordon for the differentiation of streptococci were applied by Andrewes and Horder to distinguish six main varieties of this micro-organism (*salivarius*, *anginosus*, *fæcalis*, *pyogenes*, *mitis*, and *equinus*). It cannot, however, be regarded as proved that these forms are all specifically different, since evidence has been brought forward by Ainley Walker and by

Beattie that under experimental conditions the typical fermentative reactions do not remain constant.

More recently a good deal of attention has been devoted to the study of their hæmolytic or non-hæmolytic properties as a means of differentiation. And important results are being obtained in the differentiation of streptococcal types by means of specific agglutinating serums.

Rabbits and mice are the laboratory animals most susceptible to the action of streptococci, but to produce pathological effects a relatively large amount must be inoculated. By passage through a series of animals the virulence of a streptococcus for that particular animal (e.g. the mouse) can be enormously increased.

An animal dying of experimental streptococcal infection will usually exhibit a local inflammation and perhaps an abscess at the site of inoculation, enlargement of the spleen, and a condition of general septicæmia. If death has been delayed for several days, metastatic abscesses will probably be found in many organs.

In man the distribution of the organisms is in some ways similar to that of the staphylococci. There is, however, usually a greater virulence in the infection, and a marked tendency to the production of rapidly spreading inflammations, as, for example, erysipelas and spreading cellulitis. The streptococci are the common causal agents of puerperal as well as of other septicæmias, and localized infections with these organisms are peculiarly liable to spread, and very frequently result in general infection. The streptococci are, moreover, a frequent cause of secondary infections in specific diseases such as diphtheria, influenza, and tuberculosis.

By inoculating horses with increasing doses of streptococci a number of antistreptococcic serums have been prepared. Experience is still insufficient to enable any just conclusion to be reached as to their value in the streptococcal infections. But very many successful results have been recorded, especially where polyvalent serums have been employed. In scarlet fever and in acute rheumatism particularly good results have been obtained by foreign observers.

Pneumococcus (Streptococcus lanceolatus, Diplococcus pneumoniæ).—This organism (Plate 2, Fig. 3, and Plate 3, Fig. 1) was first observed by Pasteur in the sputum of a case of rabies. He prepared pure cultures and showed that they produced septicæmia in rabbits. Talamon discovered a similar coccus in the exudation of croupous pneumonia, and shortly after Fränkel proved the identity of the two micro-organisms in question. In the following year (1886) Fränkel and Weichselbaum succeeded in clearly establishing the position of the organism as the common cause of croupous (lobar) pneumonia in the human subject. The organism

is a rounded, usually somewhat lanceolate, paired coccus, having a diameter of about 1 μ. It frequently appears in the form of short chains of four to six individuals when found in the body fluids, and in bouillon culture it may be, morphologically, quite indistinguishable from a streptococcus. In the diplococcal form the sides facing each other are often flattened, the outer sides being shaped like lancet points, and hence the organism is termed "lanceolate." In the body fluids it usually presents a well-marked capsule, but this is absent when it is grown in bouillon, and very frequently also in the case of other artificial media. It is non-motile, and has no flagella. It stains well with ordinary basic aniline dyes. It is Gram-positive, and in Gram-preparations the capsule can be counterstained by eosin.

It is aerobic, and a facultative anaerobe. Its optimum temperature is about 37° C., and its limits of growth are from about 24° C. or 25° C. to 42° C. It is soluble in bile.

In artificial culture it is very similar to the *Streptococcus pyogenes*, but usually more delicate. In bouillon, growth appears as a faint turbidity with a slight powdery deposit at the foot of the tube. Lactic acid is produced. In specially prepared gelatin (15 to 20 per cent.) which remains solid up to 25° C., small, rounded, greyish, separate colonies appear along the stab. There is no surface growth. On the surface of agar or blood-serum the culture exhibits a scarcely visible film of tiny discrete and transulcent colonies like minute dewdrops. Milk is usually coagulated. On potato visible growth does not occur.

Blood-agar is the most convenient medium for continued culture, especially if the virulence is to be maintained. The addition of from ½ to 1 per cent. of glucose to the ordinary media causes a very rapid and abundant growth of the pneumococcus, which, however, very quickly dies out under these conditions unless transplanted daily. On all media the organism dies out in a few days if not transplanted, and it soon loses virulence, except in blood-agar cultures, unless it is frequently passed through the body of a susceptible animal. But sealed up in a capsule containing fluid blood it will live and maintain virulence for a considerable time (weeks or even months).

It is killed by heating for ten minutes at 52° C. in a fluid medium, and by 1 : 20,000 corrosive sublimate solution within two hours.

The organism has a remarkably powerful hæmolytic action on red corpuscles, and produces toxic bodies of an unknown character. It is extremely pathogenetic for the rabbit and the mouse, but very slightly so for guinea-pigs and rats. Pigeons and fowls are quite immune.

In the susceptible animals there is usually comparatively little local reaction, since a condition of septicæmia is rapidly produced, and the animal dies in the course of one or two days. Post mortem

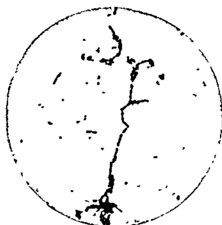


Fig. 1—Pneumococcus in sputum, growing in chains. Stained by Gram's method × 750

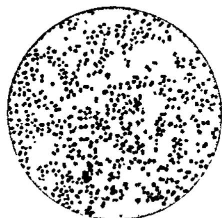


Fig 2.—Meningococcus from pure culture. Stained with carbol-fuchsin. × 1,200



Fig 3—Gonococcus in pus from acute gonorrhœa. Stained with neutral red. × 750.

PLATE 3.

the spleen is very large and hard, and the blood contains large numbers of the micro-organisms. If an attenuated culture be employed, and death be delayed, there may be a development of marked local inflammation with abscess-formation or a phlegmonous condition, and an extensive fibrinous exudation.

In man the organism is frequently present in the healthy mouth and pharynx. Under suitable conditions it may gain entrance into the lung and there produce lobar pneumonia. It can usually also be isolated from the secondary complications of this condition, such as empyema, pericarditis, endocarditis, and meningitis. It is a not infrequent cause of *acute peritonitis*, but the patients usually recover if operated on early, in marked contrast with cases of peritonitis caused by streptococci. This fact enhances the importance of an accurate bacteriological diagnosis. The infection often reaches the peritoneum from the vermiform appendix, but in a number of cases spreads to it through the diaphragm from the pleural cavity.

Antipneumococcic serums have been prepared by many investigators. They remained, in general, of little therapeutic value until within the last few years, when it has been shown, particularly by American workers, that several distinct types of pneumococci exist, and that to be effective the serum used must be specific to the particular type concerned. The use of such serums now seems to be of definite, and sometimes striking, value. This entails a careful bacteriological diagnosis of the type concerned in each individual infection.

Diplococcus intracellularis meningitidis (meningococcus).—This organism (Plate 3, Fig. 2) was first described and isolated by Weichselbaum from a number of cases of epidemic cerebrospinal meningitis. It is the causal agent of that disease. It is most commonly found within the cells of the inflammatory exudate, and hence has obtained the name "intracellularis."

The coccus varies remarkably in size even in the same culture, but on an average its diameter is 0.5–1 μ. It usually appears in the form of a diplococcus, but may at times be found occurring in tetrads. In the diplococcal arrangement the neighbouring sides of the two cocci are considerably flattened, and the organisms have the shape of coffee-beans, in this respect resembling the gonococcus. It is noncapsulated, non-flagellated, and non-motile. It stains readily with ordinary basic aniline dyes, but different individuals in the same film stain very differently. Usually the larger and the smaller cocci are only feebly stained, while those of average size stain very deeply. It is Gram-negative.

The organism is not always easy to cultivate, but when established in artificial culture it usually grows fairly well on the ordinary

media at 37° C. It is aerobic, and will not grow in the absence of oxygen. It develops *much more freely on the addition* of glucose (2 per cent.) to the media, and grows even better on the surface of serum-agar. In bouillon it produces a slight turbidity, and exhibits a tendency to form a surface pellicle. A small deposit appears at the foot of the tube.

In gelatin at 22° C. no growth occurs. On an agar-slope there is a fair growth of small, greyish, shiny colonies which sometimes gradually assume a yellowish tinge. In a *stab-culture, growth appears along* the track of the needle, decreasing rapidly from above downwards, and there is a free growth on the surface round the point of puncture. This latter feature is of value as a distinguishing character between this organism and the streptococcus and pneumococcus; it is, however, shared by the gonococcus.

On serum-agar, growth is much richer than on a simple agar-slope, and within 24 hours colonies may reach a diameter of 2–4 mm.

The organism grows well in milk, and does not cause coagulation of the casein. It usually also grows fairly well on the surface of potato at 37° C., and after some days develops a distinctly yellowish-brown hue. *Its optimum temperature is about 37° C., and its limits of* growth are from 25° C. to 42° C. It is killed by heating at 65° C. for half an hour, or by a few minutes' exposure at 80° C. It is extremely sensitive to drying, and also to the action of formalin in weak solutions (1 : 20,000). In artificial culture it dies out very rapidly unless transplanted at least once a day.

It is only slightly pathogenetic for animals; but several observers have succeeded in producing cerebro-spinal meningitis in the goat and monkey by inoculating cultures into the spinal canal.

In the human subject it is found in cases of the disease in the pus which covers the meninges and in the fluid taken by a lumbar puncture. *It is therefore of the very greatest importance in cases of doubtful* meningeal symptoms that a diagnostic lumbar puncture should be carried out, and the fluid carefully examined for bacteria.

The disease is transmitted by "carriers" who harbour the organism in the naso-pharynx, whence it may be cultivated by taking swabs with due precaution (West's tubes) against contact with saliva, which is strongly inimical to its growth. Primary cultures are best made on warmed legumin-trypsin-agar (Gordon).

Different types of meningococci have been shown to exhibit marked serological difference, and have been classified accordingly. They are identified by agglutination and absorption tests with type serums. *Antiserums* have also been prepared against the several types, and have been strongly recommended as giving the best therapeutic results. To what extent the different types described really

represent true varieties, or whether they arise to some extent by environmental modification, is still open to question.

The organism requires to be distinguished from certain other Gram-negative cocci which may be encountered in similar situations and are morphologically indistinguishable from it. These cocci are particularly *Micrococcus catarrhalis*, the *Gonococcus*, *M. pharyngis siccus*, and *M. flavus*. The last is easily distinguished by its colour. *M. catarrhalis* and *M. pharyngis siccus* grow quite well from 23° C.,

table, where the sign "plus" indicates fermentation and "nought" absence of fermentative action:—

	Glucose	*Maltose*	*Saccharose*
Meningococcus ..	+	+	0
Gonococcus ..	+	0	0
M. catarrhalis ..	0	0	0
M. pharyngis siccus	+	+	+

Micrococcus catarrhalis.—This organism is morphologically closely similar to the meningococcus But it grows readily on ordinary media, both at room-temperature and at 37° C. On agar it forms small greyish colonies, and it does not liquefy gelatin. Unless transplanted every second or third day it speedily dies out in cultivation. It ferments none of the ordinary test-sugars. It is Gram-negative.

The micro-organism has been isolated in a number of cases of bronchitis and broncho-pneumonia which otherwise presented the appearance of a mild "influenza," and it is often found associated with whooping-cough and other conditions. It is regarded as a common cause of ordinary coryza.

Gonococcus (Micrococcus gonorrhœæ).—This coccus (Plate 3, Fig. 3) was first described by Neisser in 1879, and was shown by him to be the causal agent of gonorrhœal infections, whether of the urethra or of the conjunctiva. Pure cultures were first obtained by Bumm on coagulated human blood-serum, and this observer clearly proved the specificity of the organism by inoculation upon the urethra of man.

The micro-organism is a diplococcus very similar in appearance to the *Diplococcus intracellularis meningitidis*, the single individuals having a bean-shaped outline and being flattened from side to side where they face each other. The pair of cocci measures 0·8–1·6 μ

in its long diameter, by 0·6–0·8 μ in width. About one-fifth of the long diameter represents the space between the two members of the diplococcus.

The gonococcus is non-motile, and has no flagella, nor does it possess a capsule.

It stains well with aqueous solutions of the ordinary basic aniline dyes, especially weak fuchsin, and particularly well with neutral red. An excellent method is to add a little neutral red to a small drop of fresh gonorrhœal pus upon a slide, and examine wet after placing a cover-glass upon the drop. The intracellular cocci are deeply stained, but the extracellular ones remain practically unstained; the former are therefore much more readily detected than in dried films even when they are only very few in number. The organism is Gram-negative.

It is aerobic, and a facultative anaerobe. It is difficult to grow, and dies out very rapidly unless transplanted daily. No growth occurs in ordinary bouillon or gelatin, but cultures are readily obtained on solidified human blood-serum or, better, on the surface of serum-agar (1 part of serum to 2–3 parts of agar) at 36° C. to 37° C. In 24 hours there appear a number of small colonies about the size of a pin's head, of a light-grey colour, more or less translucent, and of a very slimy and tenacious consistency. The colonies always remain discrete, *and never fuse together into a continuous film. As the colonies get* older they may assume a slightly yellowish tinge by reflected light, but at this stage the cocci are already for the most part dead.

In ascites-bouillon (ascitic fluid 1 part, bouillon 2 parts) growth occurs in the form of a fine wrinkled pellicle with a few flocculi deposited at the foot of the tube, the fluid remaining clear and free from growth.

On ordinary agar, cultures can be obtained if the medium is made just definitely alkaline to litmus, but the growth is less copious than on the special media already mentioned.

The only sugar fermented by the gonococcus is glucose (*see* Meningococcus, p. 71).

The optimum temperature is 36°–37° C., and the limits of growth from 30° C. to about 40° C. The organism is destroyed in a few hours by exposure to a temperature of 42° C. It dies out quickly in culture if not frequently transplanted, and is particularly sensitive to lack of moisture, so that when dried up it succumbs within an hour; but *in a moist condition it may remain* alive and virulent for as long as 24 hours, as for example in the water of a bath.

It is very quickly destroyed by almost all the usual antiseptics, and especially by various silver salts. A 1:4,000 solution of silver nitrate kills it within 10 minutes.

The organism produces toxic symptoms, but little of importance has been definitely ascertained with regard to the nature of the



Fig 1 — Bacillus anthracis from pure culture, showing commencing sporulation. Stained with methylene-blue. × 750.



Fig 2 — Bacillus anthracis in scraping from spleen Stained by Gram's method × 750

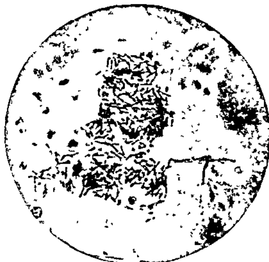


Fig 3 — Bacillus anthracis in section of liver Stained by Gram's method. × 900.

PLATE 4.

toxins themselves, though there is little doubt that they are intra-cellular in character, and are only liberated by the disintegration of the organism.

The gonococcus is practically non-pathogenetic for animals, though by the inoculation of very large amounts a localized and temporary inflammation may be produced. In man it is the cause of acute gonorrhœa, as well as of the secondary manifestations of this disease. In the acute form of the urethral infection the organism is present in large numbers in the pus, and especially within the cells themselves, both in the leucocytes and in the desquamated epithelium in the early stages of the disease. In treated individuals and in chronic cases the cocci are chiefly extracellular, and very few indeed may be found within the cells.

The infection usually remains localized in the genito-urinary tract. It may invade the posterior urethra in the male, or the uterus and Fallopian tubes in the female subject. In children the vagina itself is also sensitive to gonorrhœal infection, though hardly ever infected in the adult. The organism sometimes reaches the blood-stream, and may then produce a gonorrhœal rheumatism by setting up secondary foci of infection in the joints, or it may actually occasion general septicæmia with acute endocarditis and other lesions.

According to Neisser, no immunity is developed in the course of any gonorrhœal infection, whether localized or general.

2. BACILLI

Bacillus anthracis (Plate 4).—This organism was first observed by Pollender in 1849, in the blood of animals which had died of anthrax. It was named by Davaine, who showed that the blood from anthrax cases produced the disease in other animals only when this bacillus was present. In 1876 Koch obtained it in pure culture [illegible] ters in detail By [illegible] hed its specificity, [illegible] r. Pasteur, more-over, introduced the practice of vaccinating animals with attenuated cultures of the micro-organism as a protective measure against the natural disease.

Owing to its large size, its spore-formation, and the ease with which it is cultivated, it has been very widely employed in the study of the general problems of bacteriology.

The organism is by far the largest of the pathogenetic bacilli, and measures 3–10 μ or more long, by 1–1·5 μ in width. Its ends are usually square and sharply cut, but they may at times be even slightly concave. In culture it grows out into filaments of indefinite length

which are composed of separate individuals linked together so as to form a characteristic streptobacillus. But in the body of an infected animal it is rarely seen in chains of more than three or four, and usually occurs as single or paired rods.

It has no flagella, and is not motile. It is capsulated when obtained from tissue fluids. In culture on artificial media, but *not* in the living body of an animal, it produces spores which are of oval shape, highly refractile, and usually placed centrally within the bacillus. The spore does not expand the rod or change its contour. Spore-formation only occurs in the presence of oxygen.

The bacillus stains well with watery solution of the ordinary basic aniline dyes. In suitable preparations the spores can easily be differentiated by staining with carbol-fuchsin, decolorizing with weak acid, and counterstaining with malachite green according to the method already described (p. 44). The spores are stained red, and the bacteria themselves are green. The bacillus is Gram-positive.

In examining blood-films or pus for this organism it is advisable to stain by Gram, and counterstain with watery eosin.

The organism is aerobic, but can grow slowly under anaerobic conditions. It grows luxuriantly on the ordinary media in the presence of oxygen.

In bouillon it produces a stringy, cotton-wool-like mass of growth which lies at the bottom of the tube, leaving the fluid clear.

In a gelatin-stab there is a disc of growth upon the surface, and a continuous line along the stab showing lateral offshoots and presenting an appearance frequently described as resembling an inverted pine-tree. This so-called "spiking" may be absent in old laboratory strains, but reappears at once if the bacillus be passed through an animal or once transplanted to the surface of blood-agar. After some days the gelatin tube exhibits a marked cone of liquefaction.

On the surface of an agar-slope there is formed a pearly-greyish, rather glistening film of a granular appearance, while isolated colonies show a wavy outline. The growth is very slimy and tenacious. Under a low power of the microscope the growing edge exhibits closely-set parallel threads of wavy growth like wet cotton-wool, often described as resembling maiden's hair or "Gorgon locks."

On potato the bacillus forms a copious, grey-white, dryish, dense and elevated layer, and spore-formation takes place very freely.

Milk is coagulated in an alkaline medium, and the coagulum is subsequently, though only slowly, peptonized. Coagulated blood-serum *is slowly liquefied.*

The optimum temperature of this bacillus is about 35° C., and its limits of growth from 12° C. to 45° C. The bacilli themselves are relatively little resistant, and, in the absence of spores, are killed by an

exposure of about an hour to a temperature of 53° C., and in less than 10 minutes at 65° C. The spores, however, possess considerable resistance both against heat and drying. They may even survive five minutes' boiling, but are killed with certainty in from 15 to 20 minutes at 100° C. When dried, the spores will live for many months. Corrosive sublimate solution 1:1,000 will generally kill them within an hour, and carbolic acid in 5-per-cent. solution kills them in 1 to 2 hours *at a temperature of 55° C., but it requires more than 10 days at the* room-temperature. The action of corrosive sublimate, on the other hand, is practically independent of the temperature within the same limits.

Although a number of observers have endeavoured to isolate the special toxic products of the anthrax bacillus both from its cultures and from the bodies of animals which have died of this infection, yet the existence of a *specific* anthrax toxin, whether intracellular or extracellular, still lacks satisfactory proof. The various poisonous substances which have been isolated by different investigators do not appear to possess specific properties, and do not on injection lead to the development of any definite or recognizable immunity against anthrax. This is the more remarkable since many of the features of the disease itself point to the action of a specific toxin, which probably belongs to the intracellular variety.

Grown in solutions of pure proteins, the organism produces various albumoses, as was shown by Sidney Martin, and it develops an alkaline reaction in the medium, which he attributed to the formation of a specific alkaloidal substance. On injection into animals the albumoses caused pyrexia, while the alkaloidal substance gave rise to a condition of local hyperæmia and œdema, and led to the death of the animal concerned. Boiling destroyed the action of the albumoses, but not that of the alkaloidal body. Martin obtained similar substances from the bodies of animals which had died from anthrax infection, and accordingly concluded that they represented the true anthrax toxins.

Marmier isolated what he regarded as the anthrax toxin from glycerine-peptone-water cultures of the bacillus grown at 20° C., and claimed that by its injection into animals in appropriate doses a development of immunity could be evoked and antitoxin produced. According to Sobernheim, however, the bulk of evidence is unfavourable to these conclusions, and it must be admitted that the pathology of anthrax intoxication is at present not at all clearly understood.

The disease is one which arises epidemically among cattle, sheep, and horses, and in some countries it is probably always endemic. In man the infection is almost invariably obtained either from the carcasses, the hides, or the blood-contaminated wool and hair of animals

which have died of the disease. It appears in various forms, of which the commonest is the so-called *malignant pustule*, but it may assume a pulmonary form (*wool-sorters' disease*) due to infection of the respiratory passages, or even give rise to *intestinal* infection. A number of intestinal cases have been noted among workers with horse-hair, who were accustomed to bite off the ends of the hair with which they worked. In these, as in the great majority of cases, the infection is transmitted by the dried spores.

Of the ordinary laboratory animals, rabbits, guinea-pigs, and particularly mice are susceptible to anthrax. A mouse will die within a day or two if inoculated with only the minutest dose of a virulent strain, and is therefore the animal commonly employed for diagnostic purposes. Post mortem there is a hæmorrhagic œdema at the site of inoculation, a greatly enlarged and hyperæmic spleen crowded with bacilli, and a large number of bacilli in the blood and the other organs.

As a rule the bacteriological diagnosis of a local infection with anthrax in man is relatively easy. In the malignant pustule, which has a somewhat characteristic appearance, the bacillus will readily be detected, and it may frequently be found in pure culture in the ring of vesicles which surrounds the central area of necrosis. In the pneumonic form of the disease the bacilli will easily be identified and cultivated from the sputum, which may also be directly inoculated into a mouse. If there be pleurisy associated with the condition the pleural fluid will be found to contain long threads of the bacilli. In the intestinal form the diagnosis is more difficult, but as a rule the organism can be isolated from the fæces.

The blood should always be most carefully examined, since experience has shown that the prognosis in anthrax remains favourable so long as the bacilli cannot be detected in the blood. If, on the other hand, a condition of septicæmia has supervened, and the bacilli are present in the circulation, the prognosis becomes extremely bad.

The introduction of the treatment of anthrax with antitoxic serum is said to have yielded excellent results in Italy, the mortality of unoperated cases being reduced from 24 per cent. to 6 per cent. in the human subject (Sclavo). Active immunization by a series of vaccines is extensively employed on the Continent for protecting cattle and sheep, and has resulted in an enormously diminished mortality from this disease.

Bacillus tuberculosis (tubercle bacillus)—The discovery of the tubercle bacillus (Plate 5) was announced by Koch in 1882. But from very early times tuberculosis had been regarded as an infectious disease (Isocrates, etc.), and in the Middle Ages the danger of infection from the handling of tuberculous material was

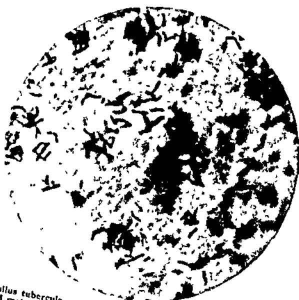


Fig 1.—Bacillus tuberculosis in section of liver Stained with carbol fuchsin and malachite-green (Ziehl-Neelsen's method) × 1,200.

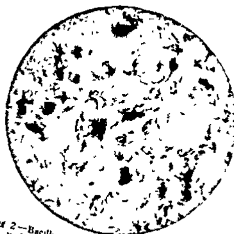


Fig 2.—Bacillus tuberculosis in sputum Stained with carbol-fuchsin and malachite-green (Ziehl-Neelsen's method) × 850

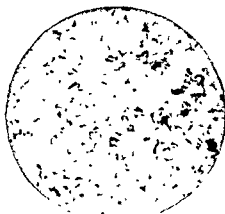


Fig 3.—Bacillus tuberculosis in section of lung. Stained with carbol-fuchsin and malachite-green (Ziehl-Neelsen's method) × 900.

PLATE 5.

clearly recognized, so that Valsalva and Morgagni were unwilling to perform autopsies on individuals who had died of phthisis.

Villemin (1865) was the first to prove conclusively that the inoculation of tuberculous material into rabbits invariably led to the development of tuberculosis in the animals in question, and that the introduction of dried phthisical sputum into their air-passages resulted in tuberculosis of the lung. These observations were extended and abundantly confirmed by the work of Armanni, of Burdon-Sanderson, and especially of Cohnheim and Salomonsen. But it was not until the publication by Koch, in 1884 (following his earlier announcement of the discovery of the tubercle bacillus in 1882), of his masterly and brilliant researches into the etiology of tuberculosis, that it was made known that the bacillus had been isolated in pure culture on artificial media, that on inoculation into animals it had produced the typical disease, and had again been isolated in pure culture from the lesions which resulted, thus finally and fully establishing both the identity and the specificity of the micro-organism in question.

The bacillus is a thin, rod-shaped organism, straight or slightly curved along its length, or even somewhat S-shaped, and often of a remarkably irregular outline. It varies considerably in length, and measures about 2–4 μ long, by 0·2 μ wide. In old cultures and in pathological material (e.g. sputum) the bacilli commonly exhibit very marked vacuolation, which produces an appearance of beading in stained specimens, and may even simulate a short chain of streptococci, owing to the fact that the vacuoles do not take up the stain.

The organism is not motile, and has no flagella. It does not form spores.

It does not stain readily with watery solutions of the ordinary basic aniline dyes, but requires special methods of staining based on the use of mordants, as in Ziehl-Neelsen's method, in Gram-staining, etc. When it has once been stained, it retains the dye with very great persistence, owing to the peculiar nature of its envelope, which contains a wax-like substance having special characters.

It is a strictly aerobic organism, but it will not grow on the ordinary media, when freshly recovered from tuberculous material, unless about 6 per cent. glycerine be added to them. It can be grown on the surface of blood-serum or serum-agar, but even in these cases the addition of glycerine greatly increases the value of the media for the human type of the bacillus.

In glycerine-bouillon it grows only on the surface, leaving the underlying fluid clear, and slowly forms a pellicle, which in the course of about five or six weeks develops into a thick and wrinkled, dry and waxy-looking membrane of a greyish-yellow colour. The culture

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produces a peculiar and distinctive aromatic smell something like that of fresh honey.

On glycerine-agar or on glycerine-serum the growth begins to appear in about 10–14 days in the form of fine, dry scales, which gradually spread over the surface of the medium. The film becomes thicker, and begins to wrinkle, and in the course of several weeks presents a heaped-up, corrugated, flaked, and broken mass of somewhat wax-like greyish-yellow or even slightly orange-coloured growth.

On glycerine-potato the organism presents a similar appearance, though the growth is rather more rapid and is usually more highly pigmented.

On special egg-media (Dorset, Besredka) the bacillus grows much more quickly, and growth becomes visible in about three to five days.

Its optimum temperature is about 37° C, and its limits of growth are from about 30° C. (22° C. or 23° C. under special conditions) to 42° C.

In a moist condition it is killed in culture within from 5 to 10 minutes at 80° C., but in sputum and other tuberculous material at least 5 minutes' boiling is required to destroy it with certainty.

In a dried condition it may remain alive and virulent for at least a year. On glycerine media its cultures live for about six months, but will certainly be dead within eight months to a year. For ordinary purposes carbolic acid is the best disinfectant of tuberculous material, while corrosive sublimate is relatively inefficient in destroying the bacilli in sputum and similar vehicles of infection. The disinfection of sputum is most satisfactorily carried out by the addition of about double its volume of 5-per-cent. carbolic-acid solution. Incidentally this procedure also improves the subsequent Ziehl-Neelsen staining of the bacilli. Direct sunlight rapidly kills the tubercle bacillus, and is one of the most efficient factors in helping to render it innocuous in nature, especially where it is present in a dried condition, as, for instance, in dust.

Certain differences in type have been shown to exist between cultures of the bacillus derived from different sources. The most important of these differences is that between the so-called "human" and "bovine" bacilli. The latter is the sole cause of tuberculosis in cattle, whereas in man, though the "human" type is responsible for the great majority of tuberculous infections, the "bovine" type also occurs, especially in children fed with milk from tuberculous cattle.

The bovine bacillus is somewhat shorter, thicker, and more uniform in size than the human type. In culture it is distinguished from the human chiefly by its scantier growth; it is therefore termed *dysgonic* (multiplying with difficulty) in contradistinction to the *eugonic* (multi-

plying easily) human type. It is also moister, less pigmented, and smoother in its growth, which is in general not favoured by the presence of glycerine. On inoculation into full-grown cattle the human tubercle bacillus produces only a local lesion. It is also less virulent for small laboratory animals than the bovine type. Both the one type and the other are virulent for guinea-pigs, and the bovine bacillus is also highly virulent for rabbits, whereas the human is only feebly so.

The products of the tubercle bacillus are of interest owing to the repeated attempts which have been made to employ them in various preparations for the treatment of tuberculous lesions in the human subject, and for the diagnosis of tuberculosis. These attempts have not at present led to clear and satisfactory results in treatment, though a number of successful cases are being recorded by observers who maintain that tuberculin as now employed yields results of undoubted value in particular forms of tuberculous infection As a *diagnostic* agent its value is certainly beyond all question; its therapeutic value is discussed in the article on the Therapeutic Applications of Bacteriology (pp. 129–30).

As first made known by Koch in 1891, *tuberculin* consisted of glycerine-bouillon cultures of the bacillus from six to eight weeks old, which were evaporated to $\frac{1}{10}$th their volume in a water-bath at 90° C. The bacilli were killed in the course of this procedure, and were subsequently filtered off. The fluid remaining was diluted and employed in the treatment of tuberculosis But the results obtained entirely failed to justify the hopes which had been formed, and the use of the tuberculin was generally abandoned, except for diagnostic purposes. For diagnosis it is still made use of in cattle, and also, to a certain extent, in the human subject. It forms a most valuable and reliable diagnostic agent. The diagnosis rests on the temporary rise in temperature of 2° or 3° F. (about 1° C.) occasioned in a tuberculous individual, but not in a normal healthy subject, by the subcutaneous injection of a small quantity of tuberculin ($\frac{1}{2}$–1 mg. in man, 30–40 cg. in cattle)

Other tuberculins containing more or less of the actual substance of triturated tubercle bacilli were subsequently prepared and investigated by Koch under the names tuberculin-O and tuberculin-R, and most recently a "New Tuberculin," which consists of an emulsion of dried tubercle bacilli ground up and suspended in equal parts of glycerine and water, and contains 5 mg. of pulverized dry tubercle bacilli per cubic centimetre.

Tuberculin-O was obtained by grinding up dried tubercle bacilli from young cultures, washing with water, and centrifugalizing. The clear fluid separated by decantation was tuberculin-O. The deposit

was again dried, ground, washed, and centrifugalized, the fluid was separated by decantation, and the whole process repeated until no deposit remained. All the fluids (except the tuberculin-O) were now mixed together, and the mixture constituted the tuberculin-R. It will thus be seen that "New Tuberculin" contains both tuberculin-O and tuberculin-R.

Tuberculin-R is still employed for the treatment of tuberculosis in man, but Koch advised the employment of the New Tuberculin for this purpose. For diagnostic inoculations, Old Tuberculin—that is to say, Koch's original preparation—should always be used.

The investigation of the specific tubercle toxins has not at present led to any very definite conclusions. They appear to be found both in the fluids of culture media and in the substance of the bacilli themselves. But it is impossible to say how far their presence in the culture fluids is due to the disintegration of bacilli which have died and become broken up in the fluid, rather than to their excretion by the living bacilli, or to processes induced in the medium by the excretion of specific ferments formed by the micro-organisms.

Many attempts have been made to produce tubercle antitoxins, and to induce the development of immunity against the tubercle bacillus in animals by injection of a variety of preparations either of the micro-organism itself or of its products. Hitherto these attempts have failed to yield any decisive results.

For the diagnosis of doubtful tuberculosis, animal inoculation is of prime importance. The suspected material should be introduced beneath the skin of a guinea-pig, preferably on the outer aspect of the upper part of the thigh. This situation ensures the early infection of the inguinal glands if living tubercle bacilli be present. The animals used must be known beforehand to be free from tuberculosis, and must be in good condition. Two guinea-pigs should be employed for each specimen of material to be tested, and they should be weighed and examined at least once a week. If the material inoculated contains living tubercle bacilli, a diagnosis can *usually* be made in from six to eight weeks, by which time typical tuberculosis, with marked loss of weight and other general signs, will have developed in the majority of cases. But if not, one of the guinea-pigs should be killed at the end of two months, and carefully examined for tuberculosis. If it is found to be quite free, a provisional negative diagnosis may be given, but the second guinea-pig must be kept under observation for at any rate six months, as cases are known in which the typical disease eventually developed although no signs whatever were present at the end of the first two or three months.

Bacillus lepræ (leprosy bacillus).—This bacillus was discovered by Armauer Hansen, who first recorded his discovery in

ditions which are to some extent unfavourable. It is not motile, and has no flagella. Spores are not formed.

The staining properties of the bacillus are somewhat unusual, and it is often said to be difficult to stain. This is due to the fact that it is very readily decolorized, unless a mordant of some kind be employed. Hence it is easily stained in a bacterial film, which only needs to be washed with water and dried off after the staining. But in sections where a dehydrating agent has to be employed, it is often decolorized, especially if alcohol be used for the dehydration.

The protoplasm of the bacillus stains irregularly, parts being deeply stained while other parts are pale, thus giving an appearance of granules and vacuoles.

In wet preparations it stains well with Czaplewski-fuchsin, or with a 0·2 per cent. solution of methylene-blue. It is Gram-negative.

The bacillus is aerobic, and a facultative anaerobe. It grows readily on all the ordinary media, better if 5 per cent. of glycerine be added, and characteristically upon the surface of potato. It prefers a slightly acid medium.

In bouillon it produces uniform turbidity, and at the foot of the tube a grey-white sediment of a distinctly slimy character. Occasionally there may be a pellicle on the surface of the fluid which is thicker at the sides than in the centre. In old cultures the bouillon acquires a yellowish-brown colour, and becomes slimy and viscous.

In gelatin there is a greyish discontinuous growth along the stab, most marked at the upper end, and on the surface a small semi-transparent disc of growth around the puncture. The medium is never liquefied.

On the surface of agar there is formed a uniform, moist-looking, slimy, greyish streak, which later on assumes a yellowish tinge.

On *potato* at the body temperature there appears an amber-coloured honey-like layer of growth, which gradually becomes darker and more opaque, passing through shades of fawn to assume in about a week a red-brown hue very similar to that of cuprous oxide. Immediately around the growth the potato itself exhibits a greenish-yellow coloration. Milk is coagulated in about a fortnight.

The optimum temperature is about 37° C., the limits of growth are 20°-43° C. It is killed within ten minutes at a temperature of 55° C. When dried, the organism will live for from two to three weeks, and in cases may be found alive even after three months. In culture it retains its vitality for considerable periods at the room temperature, and a glycerine-bouillon culture kept at a low temperature was found alive after four years. On potato it will usually die out within three or four months. It is very easily destroyed by antiseptics. Thus,

corrosive sublimate in 1 : 5,000 solution kills it in about two minutes, and 5-per-cent. carbolic acid in five minutes.

The *Bacillus mallei* produces powerful toxins which are set free into the culture media, but also exist within the bodies of the micro-organisms. Various preparations of these poisonous substances are manufactured under the name of *mallein*, either by the filtration of glycerine-bouillon cultures, or by heating the bacterial growth from the surface of potatoes in dilute glycerine or in water, and subsequently filtering off the bacteria; *or simply in the form of glycerine-bouillon* cultures sterilized by heating at 120° C.

One of the simplest and most satisfactory methods is to grow the organism for one month at 37° C. in glycerine-bouillon, which is then sterilized at 110° C. The fluid is next evaporated in a water-bath to one-tenth of its original volume, and filtered. For use it is diluted to a suitable strength with ½-per-cent carbolic-acid solution. Mallein thus prepared is used as a *diagnostic test in animals*, since it is found that the injection of a small amount of this substance produces only slight effects in normal animals, but leads to local swelling and a marked rise of temperature in animals suffering from glanders infection. The quantity of toxin to be used is determined by test observations upon horses. The dose selected is the largest amount which can be inoculated into a normal animal without producing more than at most a very slight reaction, and the strong toxin is diluted as above described, so that this quantity may be contained in a convenient volume of the fluid. The test, if carried out with due precautions, is practically always found to give a reliable diagnosis.

Mallein has also been used as a *therapeutic* agent in the treatment of glanders, in both animals and man, being employed after the manner of a vaccine as a means of stimulating the reaction of the tissues, and leading to the rapid development of active immunity. Up to the present, however, the results recorded are too contradictory to justify a definite statement as to the value of this method of treatment.

The preparation of antitoxic serums has also been attempted, but no results of practical value have hitherto been obtained.

The *Bacillus mallei* is pathogenetic for a large number of animals and for man. Inoculated subcutaneously in the horse, it produces a characteristic attack of the disease. Of laboratory animals the *guinea-pig is the most susceptible, and should always be employed* for diagnostic purposes. The suspected material is inoculated intraperitoneally in a male guinea-pig, and if the bacillus is present there rapidly occurs a purulent inflammation of the tunica vaginalis and testicles, and death usually takes place in about seven to fourteen days, from generalization of the infection.

As it occurs in man, glanders infection is usually acquired from

the horse, especially by contact with discharges from the nose, or from the ulceration of "farcy buds." The bacillus gains an entrance either through the respiratory mucous membrane or through an abrasion of the skin, and may produce either an acute infection or a chronic form of the disease. Glanders has repeatedly occurred in man with fatal results following accidental inoculations with pure cultures of the organism during laboratory investigations.

Bacillus tetani (Plate 6, Fig. 1).—The infective nature of tetanus was first clearly proved by Carle and Rattone, who showed in 1884 that the inoculation of material from the neighbourhood of the wound in a case of tetanus led to the development of the disease in the animals employed (rabbits). Nicolaier, in 1885, infected small animals with garden soil, and found that many of them developed symptoms of tetanus. When these occurred there was always found at the site of inoculation a particular thin rod-shaped organism, which Nicolaier regarded as the probable cause of the disease. He succeeded in growing the bacillus, and noted its formation of terminal spores, but did not obtain pure cultures Rosenbach demonstrated the presence of the bacillus in a tetanus wound in man, and produced tetanus in animals by inoculating them with the wound secretion, subsequently discovering the same bacillus at the site of infection in the animals in question.

In 1889 Kitasato isolated the organism in pure culture by first heating the material in which it was present for an hour at 80° C., and subsequently cultivating anaerobically on agar-plates. He showed that the inoculation of pure cultures into animals produced the specific disease, and that the bacillus could again be recovered in pure culture from the site of inoculation.

The organism is a slender rod with rounded ends, 2–4 μ long by 0·3–0 5 μ wide, which sometimes grows out into long filaments in artificial culture media. It is slowly motile, and possesses very numerous flagella, which are distributed all round its periphery (peritrichate). It forms a terminal spore whose diameter is considerably greater than that of the bacillus (1–1·5 μ), thus giving rise to the characteristic "drumstick" appearance. The spore itself is usually spherical in shape, but sometimes assumes a distinctly oval outline.

The bacillus stains readily with all the ordinary basic aniline dyes, both in wet preparations and in dried films. The spores stain easily by the modified Ziehl-Neelsen method already described, and they retain the stain in Gram-preparations. The bacillus itself is also Gram-positive.

It is anaerobic, but, though sometimes regarded as a particularly strict anaerobe, it will as a matter of fact grow very well where the conditions are only moderately anaerobic, as in a deep agar-stab,

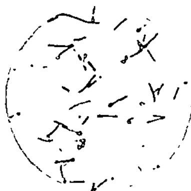


Fig 1 —Bacillus tetani from pure culture Stained by Gram's method × 1 000

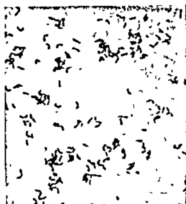


Fig 2 —Bacillus diphtheriæ from pure culture. Stained by Gram's method × 900

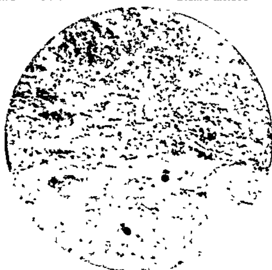


Fig 3 —Bacillus diphtheriæ in section of diphtheritic membrane Stained by Gram's method × 750



Fig 4 —Bacillus pestis in section of lung Stained with neutral red × 750

PLATE 6

where growth occurs from about 2 cm. below the surface downwards. At the same time, a relatively small amount of oxygen is sufficient to prevent all visible growth. It is therefore an advantage that about 2 per cent. of glucose should be added to the culture media in the case of this organism in order to remove any oxygen which may be taken up during the manipulation of the tubes. The tubes should also always be freshly autoclaved or boiled immediately before use, to drive out absorbed air. In the case of gelatin and agar which are melted by this process, the media should be rapidly solidified for use by placing the tubes on ice or in cold water.

In bouillon the tetanus bacillus produces a uniform turbidity, which after three or four days settles down as a powdery deposit, leaving the fluid clear. In the young culture the bacilli are for the most part single, but, as it gets older, longer and longer threads appear in abundance and very few single organisms remain. There is a *considerable* production of gas.

In a gelatin-stab (anaerobic) there is arborescent growth along the line of puncture and spreading laterally from it The gelatin is slowly liquefied, the liquefaction becoming visible along the stab in about a week at 22° C., and *gas is formed* The gas-production of this organism is important and must be emphasized, since for some reason it has often been said that gas is not produced in a pure culture. As a matter of fact, the formation of gas is one of the characteristic features of pure tetanus cultures, especially when grown in glucose media. The gas consists mainly of a number of hydrocarbons (methane, ethylene, etc.) and carbonic acid, with various other volatile bodies of offensive odour which produce a smell somewhat resembling that of burnt feathers.

In an agar-stab the growth is very similar to that in gelatin, but more rapid (at 37° C.), and the medium is of course not liquefied, but may be split up by the gas-formation

In coagulated blood-serum some strains of the organism produce slow liquefaction, while others do not.

The bacillus grows readily in milk without producing acid or leading to coagulation of the medium.

In Robertson's meat medium it forms gas, and produces no blackening of the meat.

Its optimum temperature is about 37° C, its limits of growth are from 14° C. to about 42° C. At 60° to 65° C. most of the vegetative forms (bacilli) are killed within half an hour, but the spores resist five minutes' boiling at 100° C. They are, however, killed by five minutes' exposure to the action of steam.

In artificial cultures spore-formation begins within 24 hours, and proceeds rapidly. The spores retain their vitality and virulence

almost indefinitely in a dried *condition if protected from the* action of light (more than eleven years, at any rate). According to Kitasato, 5-per-cent. carbolic acid kills them in about 15 hours, and 1 : 1,000 corrosive-sublimate solution in three hours.

The organism is very widely distributed, and is a common saprophyte in cultivated ground, in stable refuse, and in the soil of towns. It is found in the dung of horses and herbivora generally as well as of some other animals. It is very frequently to be found in garden soil. Although an anaerobic organism, it can develop in these situations since the presence of numerous aerobic forms removes the free oxygen *sufficiently to enable it to grow.*

The toxins of tetanus have been very carefully investigated. Even before pure cultures of the bacillus had been obtained, Knud Faber showed that the *bacterium-free filtrate of impure tetanus cultures* would produce the characteristic symptoms of the disease. After the micro-organism had been successfully isolated by Kitasato, numerous experiments on its toxins were carried out by many observers. The main results established may be stated as follows: In suitable media the bacillus produces toxins of such remarkable potency that even $\frac{1}{1000000}$ c.c. (one-millionth c.c.) of the filtered culture fluid may be sufficient to cause typical tetanus and death in a mouse of about 10 grm. The fluid contains at least two poisonous bodies, one of which produces the tetanic spasms (tetano-spastin), while the *other acts as a strong hæmolytic agent (tetano-lysin).* The *latter* is a very labile substance, and can only be preserved in a dried condition. It loses its activity very rapidly when present in solution, and may become practically inactive after a few hours' exposure at 37° C. The former, which is the specific toxin, is also unusually susceptible to the action of heat, so that exposure for a few minutes at 65° C., or for an hour and a half at 55° C., renders it practically incapable of producing symptoms. On the other hand, when it has been completely dried its activity is only slightly reduced by heating for an hour at 120° C. In this condition it also withstands the action of alcohol, chloroform, and ether.

On injection into animals, the tetano-toxin has a definite incubation period, but its precise duration is dependent both on the dosage and on the variety of animal employed. Even with very large doses, in the mouse, specific symptoms of intoxication do not begin to appear until after the lapse of about eight or ten hours. The toxin travels by the motor nerves to reach the cells of the anterior horn of the spinal cord, and *it has been suggested that it is absorbed in the* first case by the motor end-plates in the muscle-fibres.

Susceptibility to tetanus toxin varies in different animals. Thus, whereas mice, rabbits, and guinea-pigs are highly susceptible, consider-

able resistance is exhibited by fowls, which require 30,000 times the dose, per gramme of body weight, sufficient to kill a mouse. The alligator appears to be immune.

Administered by the mouth, the toxin produces no effect on animals, and is not absorbed in the alimentary canal. Feeding with living tetanus bacilli or spores is equally ineffective in producing the disease.

The effect of the inoculation of pure cultures into animals depends on the accompanying conditions. If a small quantity of a bouillon culture be injected subcutaneously in a mouse, the animal may be killed by the preformed toxin actually present in the fluid injected, without any development of tetanus bacilli at the site of inoculation. But if washed micro-organisms be introduced, no pathological results ensue, unless at the same time anaerobic conditions are produced at the site of inoculation, either by the association of aerobic organisms or by a local tissue injury sufficient to produce an area of cell degeneration and necrosis. This explains the fact that though the tetanus bacillus is so widely distributed, and injuries contaminated with soil are so extremely common, yet tetanus resulting from such injuries is in most places relatively infrequent.

In a case of tetanus, whether in an animal or in man, the bacillus never spreads beyond the site of primary infection, or possibly the nearest lymphatic glands. It will be found, sometimes in considerable numbers, in the pus and in the necrotic tissue of the wound, and may be recognized without much difficulty. The diagnosis should, however, always be confirmed, where possible, by the subcutaneous inoculation of a mouse with material from the wound. The symptoms of the disease are entirely toxic, and the local action on the tissue is practically negligible. The site of infection is to be regarded merely as a manufactory for the toxin, which diffuses out from it to reach the nerves and the circulating blood, and is thus carried to the central nervous system.

By appropriate and repeated inoculations of tetanus toxin into animals an antitoxic serum is readily obtained, and for this purpose the horse is commonly employed. But as the toxin is so extremely virulent, it has been found convenient to begin the immunization with a toxin diminished in activity by treatment with iodine terchloride or pure iodine. An antitoxin of great potency can thus be obtained. The antitoxic strength of any given serum is estimated in terms of an arbitrary antitoxin unit. The American unit is determined on guinea-pigs, the German unit on mice. The former is that minimal amount of antitoxin which, when mixed with one "test dose" of standard toxin, just protects a guinea-pig against the lethal effect of the toxin for at least four days.

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that it did not in fact produce a septicæmia in the living animal, as Pasteur thought, but was only to be found in the circulation after the animals had been dead for some time. It became of interest in the pathology of man in 1882, when Brieger and Ehrlich recorded two fatal cases of human infection following the hypodermic injection of a drug. Subsequently a considerable number of cases were recorded in the human subject, and infections with this organism were extremely frequent during the War.

The bacillus is a rod-shaped spore-forming organism about 3 μ long by 1 μ wide, with rounded ends, occurring singly or in chains of two or three, but frequently growing out into undivided filaments of considerable length. It is feebly motile, and possesses numerous flagella, which frequently are grouped together near one end, and project like a many-stranded whip-lash, or a sheaf of ribbon, from a staff. It produces spores which are roughly oval or egg-shaped, and are usually situated near the middle of the rod, though not uncommonly they may be found nearer one end. They are only present in the short rods, and are never seen in the long filaments. The spore distends the rod, altering its outline, so that it assumes a spindle-shaped or pear-shaped form. Sporing occurs not only in artificial cultures, but also in the œdematous exudation of infected individuals.

The organism stains well with watery solutions of the ordinary basic aniline dyes. And the spores are readily stained by the usual method (*see* p. 41).

The bacillus is Gram-positive, but it is somewhat easily decolorized. This fact may perhaps explain the divergence of opinion as to the Gram-reaction of this organism expressed by different observers. But if amyl-alcohol be used for differentiating instead of the ordinary ethyl-alcohol, a positive Gram-stain is always obtained. It seems indubitable, however, that under the name *Bacillus œdematis maligni* several nearly related organisms possessing similar characters and pathogenetic action were formerly grouped together, or actually mistaken for each other, by different investigators; and to this fact are probably in part attributable the differences in the descriptions of various authors, and perhaps also the difference of opinion as regards Gram-staining.

The bacillus is strictly anaerobic, and will only grow when oxygen is rigidly excluded. Ordinary culture media should be made with 2 per cent. of glucose, should be freshly heated before use, to drive out absorbed air, and should be kept in an atmosphere free from oxygen during cultivation; or Robertson's meat medium may be used with a layer of sterile liquid paraffin (B.P.) or vaselin on the surface.

In bouillon the bacillus of malignant œdema produces uniform

made up to a volume of 4 c.c. It is allowed to stand at room temperature for one hour, and is then injected beneath the skin of the abdomen into the guinea-pig.

The German unit of antitoxin is much larger, and is equivalent to some 60–70 American units. (The quantities given in the text *below refer to American units.*) *A serum containing anything between* 400 and 800 American units of antitoxin per cubic centimetre of volume is to be regarded as a very powerful serum.

The use of the serum, both prophylactically and therapeutically, is fully discussed in the article on Tetanus (p. 927).

In making an intrathecal injection of antitoxic serum, as much cerebro-spinal fluid should first be allowed to escape as can be removed without involving danger to the patient from an undue reduction of the intracerebral pressure, and the antitoxin subsequently injected. The withdrawal of cerebro-spinal fluid is of great importance, both because this fluid contains considerable quantities of tetanus toxin which are thus got rid of, and from the fact that otherwise the rapid introduction of the antitoxic serum might dangerously increase the subdural pressure. Following this method, an amount of between 10 and 20 c c. of the serum can safely be injected, and a good antitoxin will contain the necessary number of units within this volume.

Intravenous and intracerebral injections have also been employed The former cannot, however, in urgent cases replace the subdural lumbar inoculation. The intracerebral method is extremely dangerous, and should be avoided, as even when successful from the surgical standpoint it gives no better results than those obtained by the method of lumbar puncture.

The prophylactic use of the antitoxin has given excellent results both in animals (horses) and in man. That is to say, by its means the percentage of tetanus cases following such injuries as are likely to have been exposed to tetanus infection has been strikingly reduced (e.g. from 16 per thousand to about 2 per thousand). Further, there is now to be obtained a dried preparation of tetanus antitoxin which may be applied directly to a wound where the *possibility of tetanus infection is feared. This preparation* has been used, on the suggestion of Calmette, as a protective dressing on the umbilical cord in new-born children in Indo-China, where 20 per cent. of new-born children were said to die of tetanus neonatorum, and it has given very satisfactory results in a striking reduction of the mortality from this disease.

Bacillus œdematis maligni (Vibrion septique).—This organism was discovered by Pasteur in 1877, and termed by him the *Vibrion septique;* it was studied again by Koch in 1881, and by him renamed the bacillus of malignant œdema. He showed

Active immunity is readily obtained by the introduction of attenuated cultures.

From filtered-bouillon cultures of the organism toxic effects may be obtained in animals, but large doses have to be used to produce the characteristic lesions which occur in the bacillary infection. The toxin appears to be a highly resistant body, and is not destroyed by heating to a temperature of 110° C.

Malignant œdema is a condition now only rarely seen (under peace conditions), but it was probably common in preantiseptic days among the cases described under such terms as gangrenous emphysema, hospital gangrene, purulent œdema, and so on. When met with, the organism is usually present as a mixed infection along with other organisms, especially the pyogenetic cocci, whose association with it helps to provide the necessary anaerobic conditions.

Anaerobic bacteria in infected wounds.—Besides the *B. tetani* and the *B. œdematis maligni*, a large number of other anaerobic bacteria are met with in wounds which have been infected with soil and other extraneous matter. The majority of them are spore-bearing bacteria, and those most commonly met with in the War were classified, as regards their morphology and biochemical activities, in the Medical Research Council's Special Report No. 39, 1919 (*see* Table on p. 92).

The committee appointed to investigate these organisms came to the conclusion that *acute gas gangrene* may result from the action of at least three members of the group, which were, in the order of their frequency, *B. welchii*, *Vibrion septique* (*B. œdematis maligni*), and *B. œdematiens*. The exact part played by other anaerobes, which may be present, in the production of gas gangrene could not be clearly defined, but it was shown that by themselves they cannot in pure culture be regarded as pathogenetic for laboratory animals.

Bacillus welchii.—This organism, which is also known as *B. aerogenes capsulatus*, *B. perfringens*, and *B. enteritidis sporogenes*, is a large bacillus, 4–8 μ long by 1–1.5 μ broad, usually straight, and having rather square-cut ends. But very short forms, long filamentous forms, and even curved rods may be met with, besides a variety of pleomorphous involution forms.

The bacillus is non-motile, and has no flagella. It possesses a capsule, which is most easily seen in exudates from infected tissues, or in cultures in media containing serum.

The bacillus stains well with the ordinary basic aniline dyes, and is Gram-positive, though in old cultures Gram-negative individuals may be found.

Spores are readily formed in artificial culture on suitable media,

turbidity with a scanty deposit, and there is a very free formation of gas, consisting of a mixture of hydrogen, carbonic acid, methane, and a number of highly odoriferous fatty and aromatic acid substances which together produce a powerful and very strikingly unpleasant smell.

In a gelatin-stab the growth appears as a row of rounded colonies, at first small and translucent, becoming, later on, fused into a white line of opaque growth presenting short lateral offshoots. The gelatin *is liquefied in a long cylinder, and gas is formed.*

In an agar-stab, growth takes place rapidly at the body temperature, and appears either as a felted network of diffuse growth along the stab, or as a series of small biconvex granulated separate colonies which become fused into a continuous white line of culture. Bubbles of gas are formed in the medium, which may be much split up as the colonies increase in size.

Milk is coagulated slowly, with the production of acid and gas.

The optimum temperature is about 37° C., but the organism grows well at the room temperature. Spore-formation takes place above 20° C., and is rapid at the body temperature. The spores resemble those of tetanus in their resistance to heat, to antiseptic action, and to drying. In dried-up tissues they retain their virulence for years.

The organism is common in the soil of cultivated areas, and wherever putrefying animal matter is present. It may usually be isolated by introducing a small amount of garden earth beneath the skin of a mouse or guinea-pig. When inoculated subcutaneously in pure culture it produces spreading œdema of a hæmorrhagic character, with moderate gas-formation in the subcutaneous tissue and the neighbouring muscles. Death usually occurs from acute intoxication in from 16 to about 24 hours. The bacilli are present in great numbers in the œdema fluid and the affected tissues, but as a rule the blood and the organs generally are entirely free. After the death of the animal, however, the whole body may be invaded by the organism *in the course of a few hours.*

Washed organisms, freed from their toxins, may be injected in small quantities without producing pathological effects if care be taken that the tissues are not bruised or injured at the site of the inoculation, the bacillus being unable to develop and produce its toxins owing to the presence of oxygen in the tissues. On the other hand, when it is injected along with its toxins, the latter, by producing cell degeneration and necrosis of tissue, provide an anaerobic focus for the development of the micro-organism. Intravenous inoculation usually produces no effect, as the organism does not develop in the oxygenated blood.

and sporing forms may at times (though not usually) be found in infected wounds. The spores are large, oval, and central or subcentral.

The bacillus is anaerobic, but not very strictly so. Its essential cultural characters are shown in the table on p. 95, compiled from the Medical Research Council Report already referred to.

Bacillus œdematiens.—This organism is a large bacillus, as thick as *B. welchii*, and usually somewhat longer. The rod is often curved, and short chains or filamentous forms are sometimes produced. The bacillus is flagellated, and is motile under strictly anaerobic conditions, though non-motile on exposure to air. It has no capsule.

It stains well with the ordinary basic aniline dyes, and is Gram-positive.

Spores are formed in all media. They are large, oval in shape, and situated centrally or subterminally.

The bacillus is *strictly* anaerobic. Its cultural characters are shown in the table on p. 95.

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Following these earlier observations, numerous investigations were carried out by Brieger and Fränkel, Löffler, Roux and Yersin, and a number of other observers, which led to a general recognition of the organism as the causal agent of diphtheria. The researches of Roux and Yersin on the action of the toxins which they obtained from cultures definitely proved the specificity of the bacillus by showing that these substances produced the general phenomena of the disease in question, and notably in many cases grave paralyses.

The bacillus is a rod-shaped organism, straight or slightly curved, of irregular outline, with swollen or pointed ends, and of very various size, measuring from about 2 μ up to some 6 or 8 μ in length, by 0·3–0·5 μ wide. Involution forms appear very early in a growing culture, and show even greater variations in shape, including what have been described as clubs and pear-shaped forms of the bacterium. They may show so much fragmentation as to present the appearance of a row of streptococci.

The organisms exhibit a marked tendency to assume a somewhat geometrical arrangement, which is frequently compared to Chinese writing; at other times they may be found in groups, radiating from a centre like the ribs of a lady's fan.

CLASSIFICATION OF ANAEROBIC BACTERIA MET WITH IN WOUNDS CONTAMINATED WITH SOIL, ETC.

	Both proteolytic and saccharolytic properties.		Slight proteolytic but no saccharolytic properties.	Saccharolytic but no proteolytic properties.	Neither saccharolytic nor proteolytic properties.
MORPHOLOGY	Proteolytic properties predominating. Coagulated serum and gelatin are liquefied.	Saccharolytic properties predominating. Serum not liquefied, gelatin liquefied.	Serum not liquefied, gelatin liquefied.	Neither serum nor gelatin liquefied.	Neither serum nor gelatin liquefied.
CENTRAL OR SUBTERMINAL SPORE	*B. sporogenes* *B. parasporogenes* *B. histolyticus* *B. aerofetidus* *B. bifermentans*	*B. welchii* *Vibrion septique* *B. chauvœi* *B. œdematiens* *B. botulinus*		*B. fallax* *B. butyricus* *B. multifermentans tenalbus*	
OVAL TERMINAL SPORE	.. ..	.. ..	.. ..	*B. tertius*	*B. cochlearius.*
SPHERICAL TERMINAL SPORE	.. ..	.. ..	*B. tetani*	*B. tetanomorphus* *B. sphenoides*	

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The bacillus is not motile, and has no flagella. It does not form spores.

It stains readily with watery solutions of the ordinary basic aniline dyes, both in dried films and in wet preparations. The latter method of examination, which was originally proposed by Salomonsen, affords the most typical picture of the organism as regards its varied shape, cross-banding, granulation, and so on. The bacillus is Gram-positive.

By special staining methods (Neisser's stain for dried films, or, better, Bie's stain with a wet preparation) it is possible to demonstrate in the bacilli, grown on serum media, the so-called Ernst-Babes granules, two or three in number in each rod, which, together with the other features of the micro-organism, are practically diagnostic of the diphtheria bacillus.

The bacillus is aerobic, and a facultative anaerobe.

In bouillon the appearances may vary very greatly; thus, there may be a general turbidity, or a turbidity with distinct granulation, or granulation alone, the fluid remaining clear. There may be more or less deposit at the foot of the tube, and there may be a pellicle of variable thickness on the surface, whether the fluid beneath be clear or turbid.

In gelatin the growth is very scanty, and there is no liquefaction of the medium. On the surface of agar there is a growth of small, greyish, isolated colonies which do not fuse. On coagulated blood-serum the bacillus grows somewhat more rapidly than most organisms likely to be associated with it in the throat, and appears in the form of small, opaque, white colonies elevated above the surface of the medium and rounded in outline. Milk is not coagulated.

The bacillus ferments glucose, but not saccharose.

Its optimum temperature is 34°-37° C., its limits of growth are about 20°-42° C. It is killed within from 5 to 10 minutes at 60° C. in a moist condition, but in the dried-up substance of diphtheritic membrane it may resist a temperature of nearly 100° C. (95° C. to 98° C.) for about an hour.

In dried diphtheritic membrane it may remain alive and virulent for three or four months. And the same statement holds for a pure culture dried upon silk threads. In ordinary culture media it survives for a considerable period, and may be found living after the lapse of from six to eighteen months. *It is somewhat resistant to the action* of antiseptics, but formaldehyde and hydrogen peroxide are specially valuable disinfectants for this organism.

The diphtheria bacillus produces a powerful toxin. This is best prepared by growing the bacillus in bouillon cultures, when it is observed that the reaction of the medium is changed from alkaline to acid in

TABLE OF CULTURAL CHARACTERS OF B. *TETANI*, B. *ŒDEMATIS MALIGNI*, B. WELCHII, AND B. ŒDEMATIENS

Name	Motility	Spores	Surface colony	Colony in agar shape	Cultural reactions in			
					Milk	Robertson's meat medium	Coagulated serum	Gelatin
B. tetani	Yes	Spherical, strictly terminal	Flat and delicate, with projections growing out at the edges	Branching and flocculent	No change	Gas; no blackening	Not liquefied	Liquefied
B. œdematis maligni (*Vibrion septique*)	Yes	Spores are formed readily in all media; they are central or subterminal	Delicate and faintly opalescent; round, sometimes with indented or crenated edges	Semi-transparent, with fern-like branchings	Acid and clot; some gas may be *formed*; slow reaction 3–6 days	Gas; pink colour which *fades* later; no blackening	Not liquefied; variations in morphology —citrons, navicular types, club-shaped forms, etc., may be developed	Liquefied
B. welchii	No	Large oval, with slightly flattened ends; central or subterminal Formed only in sugar-free media rich in protein, such as coagulated serum, alkaline egg fluid, and casein broth	Round with smooth edges	Opaque and lenticular	Stormy fermentation; very rapid clotting, torn with gas; acid reaction	Gas; pink colour; sharp *butyric acid* odour; no blackening	Not liquefied; spores formed; filaments and involution forms occur	Liquefied
B. œdematiens	Only motile under strictly anaerobic conditions	Spores formed in all media; oval, with slightly flattened ends; central or subterminal	Flat, and inclined to be confluent; growing out in finger-like processes	Transparent snow-flake colonies, sometimes with opaque centres	Acid after 4 to 6 days, slight clotting after some weeks	Gas; no blackening; pink colour at first, then bleached	Not liquefied	Liquefied

the course of a few days, but subsequently again becomes alkaline. After three or four weeks' growth at 35° C., the fluid is filtered off from the bacteria, and is found to possess a highly toxic action for animals. The toxin is moderately susceptible to the action of heat, and in a moist condition rapidly deteriorates at a temperature of 60° C. It is speedily rendered inactive by exposure to 100° C. In a dried state it can withstand heating at 100° C. for a quarter of an hour without appreciable injury. The strength of the toxin is usually tested on guinea-pigs, and is measured in multiples of the smallest dose which kills a guinea-pig weighing 250 grm. within three or four days

On subcutaneous injection of the toxin into guinea-pigs characteristic pathological changes are produced, which differ somewhat according as a minimal lethal dose or less than this amount is introduced. *In the former case there is developed at the site of inoculation in the* course of a day or two (if the animal does not die within this period) an extensive and somewhat hæmorrhagic œdematous infiltration.

In the peritoneal, pleural, and pericardial cavities is usually found a larger or smaller amount of serous exudation. In the lungs are often present areas of hæmorrhagic consolidation, and the suprarenal capsules show a deep, almost magenta-red condition of congestion, and may exhibit interstitial hæmorrhages. There are pronounced fatty changes in most of the parenchymatous organs.

Where a smaller dose of the toxin has been given and the animal survives, the local infiltration following the injection may spread very widely, and becomes very hard and indurated in the course of some three or four days. The hair falls off, and a large area of necrosis may be produced. The ulcer which results from the separation of the dead material may gradually heal up, and the animal then apparently recovers. But in a number of cases paralytic symptoms manifest themselves from about the sixteenth to the twenty-fourth day, or even later. The paralysis begins in the hind limbs, and spreads upwards, leading to the death of the animal in many instances.

If living cultures of the diphtheria bacillus be inoculated into guinea-pigs, the effects produced are very similar to those which follow the injection of the bacterium-free toxin. The bacilli themselves are, with quite rare exceptions, only found at the site of inoculation, and even here they begin to decrease in number after a few days.

In man the bacilli are present in great numbers in the false membrane of diphtheritic lesions in the pharynx, or wherever they are situated. But their discovery in the circulation and the internal organs is extremely rare. It is important to remember that quite virulent organisms may long remain in the throat after complete recovery from the disease, and are not infrequently present in the throats of healthy persons, who may act as "carriers" of infection.

This disease, like tetanus, is a toxæmia, and can be combated by the use of antitoxin. Antitoxic serums are produced by the systematic and repeated injection into the horse of graduated doses of diphtheria toxin. The antitoxin was originally standardized by determining the amount which would protect a guinea-pig of 250 grm. weight against an amount of toxin corresponding to 100 lethal doses, and this amount was taken as the unit of antitoxin. In practice it is now usual to standardize all antidiphtheritic serums by comparison with a standard serum originally prepared by Ehrlich.

As a rule the best serum contains about 400 to 800 antitoxin units per cubic centimetre. In using it as a therapeutic agent in human diphtheria large doses should be given at the earliest possible moment. Indeed, some authorities now administer, in severe cases, as much as 50,000 to 100,000 units, or more, intravenously within the first two days

There is still a tendency, as in the case of tetanus antitoxin, to administer the remedy in insufficient amounts As a prophylactic agent during epidemics of diphtheria a single dose of about 2,000 to 4,000 units is appropriate. Statistics show that where this method of protection has been extensively employed among school children, both the incidence and the severity of the disease are greatly reduced.

Pseudo-diphtheria bacillus (Hoffmann's bacillus). —This bacillus, observed by Löffler in 1887, and fully described and cultivated by Hoffmann in 1888, is only of importance in that it may sometimes be mistaken for the diphtheria bacillus. It is often found in the throats of healthy persons as well as in association with diseased conditions The main points of difference which suffice to distinguish it from the true diphtheria bacillus may be enumerated as follows :—

It grows readily on the same media as the diphtheria bacillus, but produces a more luxuriant, whiter (with ultimately a yellowish tinge), and more opaque growth.

It also grows in gelatin even at 18° C. In bouillon it produces no acidity at any period of its growth, and it does not ferment glucose.

Its cultures are non-virulent for guinea-pigs.

Morphologically it is somewhat shorter and thicker, and more uniformly and deeply staining, than the diphtheria bacillus, and exhibits less variety of form and size. When stained by Bie's or Neisser's method it does not usually present the Ernst-Babes granules, and with the ordinary stains the beading or granulation of its protoplasm is much less marked than in the case of true diphtheria. It is Gram-positive.

Where the diagnosis otherwise remains in doubt a guinea-pig should be inoculated subcutaneously.

Bacillus influenzæ.—This bacillus was discovered almost simultaneously by Pfeiffer, Kitasato, and Canon, in 1892. It was first cultivated on artificial media by Pfeiffer, to whom we chiefly owe the original exact investigation of the organism.

The bacillus is of surgical interest as an occasional cause of otitis media, of suppurative *meningitis*, of *appendicitis*, and of an acute urethritis closely simulating gonorrhœa.

It is a tiny rod measuring from 0.5 μ to 1 or 1·5 μ in length by about 0.2 *to* 0·3 μ *in* breadth, quite straight, with conical blunt ends, and usually arranged in pairs which are aggregated together into larger or smaller masses. It is not motile, and has no flagella. *It does not form spores.*

It stains fairly well though somewhat faintly with the ordinary basic aniline dyes, and shows a tendency to exhibit polar staining. *It is Gram-negative.*

It does not grow on the ordinary media unless either blood or hæmoglobin has been added. It is strictly aerobic. Grown on the *surface of blood-agar at* 37° C., *it produces in about* 24 *hours tiny* discrete, greyish, circular colonies like drops of dew. The colonies do not fuse, and never exceed the size of a pin's head.

The *bacillus does not grow below* 25° *C.*, *and its maximum limit* is about 42° C. or 43° C., with an optimum at 37° C. It exhibits very low resistance to external agencies, and is destroyed in about 5 minutes at 60° C. When dried up it dies in less than 24 hours, and in fluid media is equally susceptible, though in moist sputum it may live for as long as from 10 to 14 days. In culture it must be transplanted every second day to ensure its continued growth.

Bacillus pestis (Plague bacillus).—This organism (Plate 6, Fig. 4), discovered independently by Yersin and Kitasato in 1894, is only of surgical interest in connexion with the buboes which are formed in ordinary cases of bubonic plague.

It is a somewhat oval, rod-shaped organism with rounded ends, of rather variable size, very similar in appearance to Ducrey's bacillus, and measuring about 1·5-2 μ long, by 0.5–0·7 μ wide. It is not motile, and has no flagella. It does not form spores. Sometimes, especially in films from pathological material, it presents the appearance of a definite capsule.

It stains readily with the ordinary basic aniline dyes, and exhibits pronounced polar staining. It is Gram-negative.

It grows well on all ordinary media at the body temperature, and growth continues down to 5° C. or 6° C.; its optimum is between 25° C. and 30° C., and its maximum about 42° C. or 43° C.

In bouillon it produces a fine granular or slightly flocculent deposit, and there may be a slight turbidity of the medium. If a little oil be

placed upon the surface of the bouillon a somewhat characteristic appearance is produced by the formation of "stalactites" of growth extending downwards from the drops of oil. In films from bouillon *cultures the organism is present in long chains.*

On the surface of agar there appears a continuous line of whitish growth, smooth and transparent, and exhibiting an irregular or wavy margin. The centre of the streak assumes a darker tinge and becomes brownish-grey. Gelatin is not liquefied.

Involution forms are rapidly produced in great variety in artificial cultures of this organism.

Bacillus pyocyaneus.—The bacillus of "blue" (bluish-green) pus was first isolated by Gessard in 1882; its pigment, pyocyanin, had already been separated from blue pus by Fordos in 1860.

The organism is a tiny slender rod with rounded ends, of very variable length, measuring from 0·6 μ to 2 μ or 3 μ, and even up to 6 μ in length, by 0·3–0·6 μ in breadth. It is very highly motile, and exhibits a single terminal flagellum. It does not form spores.

It stains readily with aqueous solutions of the ordinary basic aniline dyes. It is Gram-negative.

It is strongly aerobic, but a facultative anaerobe. When grown aerobically it rapidly produces a highly fluorescent blue-green colouring matter which becomes diffused into the surrounding medium, but under anaerobic conditions the growth remains completely colourless.

The bacillus grows readily on all the ordinary media with the production of pigment. In bouillon it produces a surface pellicle and marked turbidity of the medium, with a dense and more or less tenacious deposit at the foot of the tube. The fluid becomes greenish and distinctly fluorescent.

In gelatin-stab a cone of liquefaction is produced containing turbid growth at the apex of the cone, and the surrounding medium assumes a greenish tinge.

On agar there appears a fairly abundant, slimy, somewhat wrinkled, greyish layer of growth accompanied by pigmentation (green), and marked fluorescence of the medium.

Milk is coagulated in the course of several days, and subsequently the coagulum is again liquefied

On potato the bacillus produces a copious, slimy, slightly olive-tinted brown layer, and might readily be mistaken on this medium for the *Bacillus mallei.*

The organism is common as a saprophyte upon the skin, in the mouth, and in the intestinal tract. It has now very little importance as regards pathogenetic action in the human subject, though in animals (especially in rabbits) it produces suppuration when inoculated experimentally, and in sufficient doses leads to the development of a

eading hæmorrhagic œdema and a condition of general septicæmia. preantiseptic days it was commonly met with as a secondary ection in suppurating wounds, causing the pus and even the bandages l dressings to assume a blue-green colour.

Bacillus typhosus (Eberth-Gaffky bacillus). — The *illus typhosus* (Plate 7) was observed by Eberth in 1880, in the spleen l in the intestinal lesions in cases of typhoid fever. Shortly after- rds its presence was demonstrated in stained sections by Koch. was isolated in pure culture by Gaffky in 1884.

It is of surgical interest as an occasional cause of abscesses and er complications occurring in the course of typhoid fever or ing convalescence.

It somewhat closely resembles the *Bacillus coli*, the chief points difference being the following: It is more rapidly motile, and has ch longer and more numerous flagella (10-12), which are peri- hate. It grows rather less freely on all media, and its cultures less dense, less granular, and more translucent than those of the *illus coli*. On the surface of potato it forms only a very delicate ourless film. In stab- or shake-cultures it never produces any

Other members of the same group are the *Bacillus paratyphosus-A* l the *B. paratyphosus-B*, which are morphologically indistinguish- e from the *Bacillus typhosus*, and produce similar, though often newhat milder, pathological conditions.

In order to differentiate between the *Bacillus coli*, the *Bacillus hosus*, and the *Bacillus paratyphosus-A* and *-B*, cultures must be de on special media, and the agglutination test with known glutinating serums must be employed where the diagnosis otherwise nains in doubt.

The following are the chief points of diagnostic value:—

Milk is coagulated by the *B. coli*, with the production of an acid ction, but not by *B typhosus* or *B. paratyphosus-A* and *-B*.

On potato the *B. coli* and the *B. paratyphosus-B* usually produce brownish-coloured growth; *B. typhosus* and *B. paratyphosus a* ourless film.

In lactose bouillon (previously freed from dextrose) *B. coli* yields abundant gas-formation and acidifies the medium, while *B. typhosus* l the paratyphoid bacilli form no gas.

In dextrose media the *B. coli* and the *B. paratyphosus-A* and *-B* se fermentation of the sugar and the formation of gas, while the *typhosus* gives no gas-formation, though acid is produced.

In neutral-red lactose bouillon (Dreyer and Fitz-Gerald),[1] within

[1] Ordinary veal bouillon, to which are added 3 per cent. of lactose and per cent. of 1-per-cent. aqueous solution of neutral red (Grübler).



Fig 1 —Bacillus typhosus from pure culture, showing long filamentous forms Stained with carbol-fuchsin. × 900



Fig 2 —Bacillus typhosus in section of intestinal ulcer Stained by Pappenheim's method. × 900.

PLATE 7.

spreading hæmorrhagic œdema and a condition of general septicæmia. In preantiseptic days it was commonly met with as a secondary infection in suppurating wounds, causing the pus and even the bandages and dressings to assume a blue-green colour.

Bacillus typhosus (Eberth-Gaffky bacillus). — The *Bacillus typhosus* (Plate 7) was observed by Eberth in 1880, in the spleen and in the intestinal lesions in cases of typhoid fever. Shortly afterwards its presence was demonstrated in stained sections by Koch. It was isolated in pure culture by Gaffky in 1884.

It is of surgical interest as an occasional cause of abscesses and other complications occurring in the course of typhoid fever or during convalescence.

It somewhat closely resembles the *Bacillus coli*, the chief points of difference being the following: It is more rapidly motile, and has much longer and more numerous flagella (10-12), which are peritrichate. It grows rather less freely on all media, and its cultures are less dense, less granular, and more translucent than those of the *Bacillus coli*. On the surface of potato it forms only a very delicate colourless film. In stab- or shake-cultures it never produces any gas

Other members of the same group are the *Bacillus paratyphosus-A* and the *B paratyphosus-B*, which are morphologically indistinguishable from the *Bacillus typhosus*, and produce similar, though often somewhat milder, pathological conditions.

In order to differentiate between the *Bacillus coli*, the *Bacillus typhosus*, and the *Bacillus paratyphosus-A* and *-B*, cultures must be made on special media, and the agglutination test with known agglutinating serums must be employed where the diagnosis otherwise remains in doubt.

The following are the chief points of diagnostic value :—

Milk is coagulated by the *B. coli*, with the production of an acid reaction, but not by *B typhosus* or *B. paratyphosus-A* and *-B.*

On potato the *B coli* and the *B. paratyphosus-B* usually produce a brownish-coloured growth ; *B. typhosus* and *B. paratyphosus* a colourless film

In lactose bouillon (previously freed from dextrose) *B. coli* yields an abundant gas-formation and acidifies the medium, while *B. typhosus* and the paratyphoid bacilli form no gas.

In dextrose media the *B. coli* and the *B. paratyphosus-A* and *-B* cause fermentation of the sugar and the formation of gas, while the *B. typhosus* gives no gas-formation, though acid is produced.

In neutral-red lactose bouillon (Dreyer and Fitz-Gerald),[1] within

[1] Ordinary veal bouillon, to which are added 3 per cent. of lactose and 0·5 per cent. of 1-per-cent. aqueous solution of neutral red (Grübler).



Fig 1 —Bacillus typhosus from pure culture, showing long filamentous forms. Stained with carbol-fuchsin × 900



Fig 2 —Bacillus typhosus in section of intestinal ulcer. Stained by Pappenheim's method. × 900.

PLATE 7.



Fig 1.—Bacillus coli from pure culture. Stained with carbol-fuchsin. × 750



Fig 2—Actinomyces from pure culture. Stained by Gram's method. × 750.



Fig 3.—Actinomyces in section of kidney. Stained by Gram's method. × 300



Fig 4.—Spironema pallidum in section of suprarenal capsule. Very numerous Stained by Levaditi's method. × 750

PLATE 8.

the first twenty-four hours at 37° C., the *B. coli* turns the medium to a pinkish-yellow colour and produces fluorescence. The *B. typhosus* changes the original iron-red colour to a deep magenta-red, the *B. paratyphosus-A* gives a cherry-red colour with fluorescence, and the *B. paratyphosus-B* renders the medium bright yellow and fluorescent. After from four to six days at the same temperature, the culture of *B. coli* has assumed a cherry-red or even a magenta-reddish hue, that of the *B. typhosus* has become yellow, that of *B. paratyphosus-A* remains cherry-red, that of *B. paratyphosus-B* remaining yellow. No further change occurs, however long the incubation of the cultures is continued. This test affords a simple and quite certain means of differentiating between the three organisms in question.

Other members of this extensive group of bacteria, such as the *B. aertrycke*, *B. enteritidis* (Gaertner), etc., and the *B. dysenteriæ* (both Shigas's and Flexner's), are not of sufficient importance from a surgical standpoint to require description here. In culture they resemble the *B. typhosus*, but the *B. dysenteriæ* gives a dark-grey or red-brown growth upon potato, thus distinguishing itself from the *B. typhosus*. The differential diagnosis of this group of organisms is shown schematically on page 102.

Each micro-organism is then examined for further confirmatory characters by means of agglutination tests carried out with specific immune serums.

Bacillus coli communis (Bacterium coli commune).—The colon bacillus (Plate 8, Fig. 1) was discovered by Escherich in 1885, following the isolation of the *Bacillus typhosus* by Gaffky in 1884. It is a normal saprophyte in the intestine, but under various conditions, including any inflammation of the intestinal wall, it may escape from the alimentary canal and exercise pathogenetic action in the tissues, especially in the neighbourhood of the intestine, in the peritoneum, and in the uro-genital apparatus

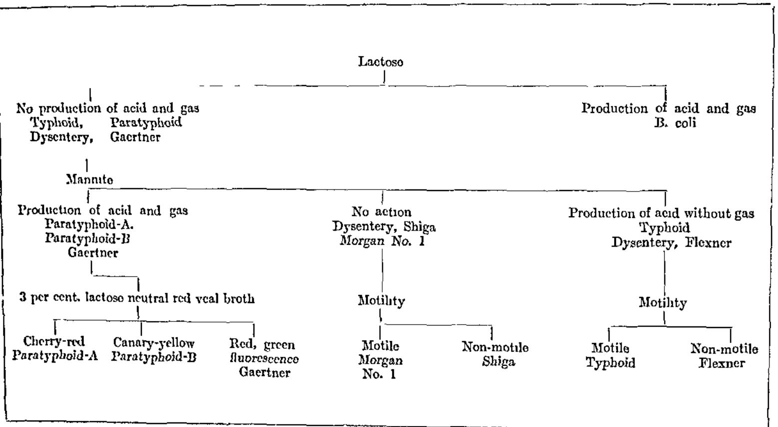
The bacillus is a rod-shaped organism, straight or slightly curved, with rounded ends, of very variable size under different cultural conditions, but measuring on an average about 2–4 μ (limits 1–5 μ) long, by 0·4–0·7 μ wide. It is motile, and has rather short flagella; it does not form spores, and does not usually exhibit any capsule.

It stains readily with aqueous solutions of the ordinary basic aniline dyes, both in dried films and in wet preparations. It is Gram-negative.

The organism is aerobic, and a facultative anaerobe. It grows well on the ordinary media.

In bouillon it rapidly produces a thick uniform turbidity and a heavy deposit. A pellicle may be formed upon the surface.

Differential Diagnosis of Typhoid, Dysentery, and Allied Bacilli



In gelatin-stab it grows freely along the puncture, and produces gas. It spreads over the surface of the medium, forming a slimy, greyish, somewhat iridescent film. There is no liquefaction of the gelatin.

On the surface of agar the bacillus forms a luxuriant, yellowish-white, shiny, iridescent, slimy-looking film.

On potato there appears a brownish layer of growth.

Milk is coagulated within two or three days, and becomes acid.

The bacillus is capable of fermenting a number of sugars, with a production of acid and gas It belongs to a large group of closely allied organisms which includes the *B. typhosus*, *B. paratyphosus-A* and *-B*, *B. dysenteriæ*, but is distinguished from them by its fermentation of lactose. The cultural differentiation of these allied micro-organisms is described under *B. typhosus*.

The optimum temperature of the bacillus coli is about 37° C, and its limits of growth are from about 6° C. or 8° C. to about 46° C. or 48° C. It is killed in from 10 to 15 minutes at 60° C. in fluid suspension. Against the effects of drying it possesses a moderate resistance, varying with the nature of the vehicle in which it is contained. Upon silk threads it may remain alive for several months in a dried condition, while on a smooth surface such as that of glass it lives for only a few days.

In culture it survives for many months without transplantation. It is more resistant to the action of most chemical disinfectants than the other members of the group, and particularly than the *B. typhosus*. One-per-cent. carbolic acid kills it within 10 minutes, and ½-per-cent. carbolic acid in about 60 minutes, while the *B. typhosus* is destroyed in 30 minutes at this latter concentration

On inoculation subcutaneously into animals in moderate doses it produces local abscesses, especially in rabbits and guinea-pigs. In larger amounts it may give rise to general septicæmia and death. Immunity is readily evoked by the repeated inoculation of small doses of the bacillus in increasing quantities.

In the human subject it may give rise to various suppurative inflammations and chronic catarrhal affections under the conditions previously mentioned.

Actinomyces (ray fungus).—This micro-organism (Plate 8, Figs. 2 and 3) was discovered in the ox by Bollinger in 1877, and in the following year Israel described it in the human subject, the identity of the two being established by the observations of Ponfick.

It appears in the form of a mycelium composed of interlacing threads of leptothrix-like growth which exhibit true branching.

In pure culture the organism presents a mycelium of this character whose branches are given off at various angles, and produce a felted

network of threads, which may or may not exhibit definite segmentation. As the age of the growth increases, segmentation becomes definite and marked, and the threads may even assume the appearance of a row of cocci. The threads are usually about 0·4–0·6 μ wide. Under moderately anaerobic conditions, club-shaped swellings may appear upon the ends of the terminal branches, *but only* in particular varieties of the fungus.

In the living body the appearances are somewhat different from those seen in cultures, and in the human subject they differ from those observed in animals. In man the organism is usually found in the pus obtained from abscesses in various organs and bone-lesions, while in cattle it is more commonly contained in fibrous nodules of a chronic inflammatory character, though abscesses may also occur in these animals. In the "*pus*" are seen in most cases a number of tiny sulphur-yellow or greyish granules, 0·2 mm. to 1 mm. or more in diameter, which on examination are found to consist of a closely interwoven mycelium presenting characteristic club-shaped swellings (true "clubs") of the extremities of the threads around the periphery of the mycelial network. In some cases, however, the mycelium does not form masses large enough to be visible to the naked eye as granules. The clubs stain differently from the rest of the colony, and the mycelial threads can then be seen to pass right up the axis of the clubs, which surrounds them in the manner of a swollen terminal sheath. Sometimes the extremity of the thread within the club is pointed, but in other cases it may be distinctly bulbous. In actinomycotic lesions in human tissues the "clubs" are difficult to stain, and have sometimes been stated to be absent. But they can usually be demonstrated by special staining methods (Wheal and Chown).

Somewhat similar appearances are seen in the fibrous nodules found in cattle, the colony exhibiting a more or less mulberry-like and granulated aspect in the mass, and on section a radiating series of blunt wedges projecting outwards from the central network and widening as they pass towards the periphery.

The actinomyces is not motile, it has no flagella, and it does not form true spores.

It stains readily with watery solutions of the ordinary basic aniline dyes. It is Gram-positive. But the clubs take the counterstain in sections from tissues, and are particularly well seen if eosin, acid fuchsin, or saffranin be used for the purpose.

The organism is aerobic, and a facultative anaerobe. But some varieties described appear to be almost completely anaerobic. It is somewhat difficult to isolate in pure culture from diseased tissues.

In bouillon it appears in the form of little granular balls of various

sizes, with an irregular and prickly-looking outline. These fall to the bottom of the tube as a deposit, leaving the fluid clear.

On the surface of agar it forms in about a week or ten days a series of more or less separate, roughly circular little masses of heaped-up growth, of a greyish-yellow colour, somewhat flaky on the surface, each colony frequently exhibiting a central dimple and the appearance of concentric rings of irregular and somewhat granulated growth. The mycelial threads penetrate beneath the surface of the medium, and the culture is therefore somewhat firmly adherent.

The optimum temperature of the micro-organism is 35°-37° C., and its limits of growth are *in some strains* from 30° C. to about 42° C., but in other varieties growth occurs as low as 15° C., or even lower.

The clinical term actinomycosis probably includes a number of different but very similar infections, in which the causal agents may be either one or other of several different varieties of actinomyces, or may be one of the less familiar streptothriceæ. The *commonest variety* of actinomyces in the human subject *grows only* in artificial culture above about 30° C, and shows a marked preference for anaerobic conditions, and may even grow only anaerobically on first isolation (Israel and Wolff, J. H. Wright). This variety is by Colebrook termed true *Actinomyces* "*bovis*" (Israel-Wolff), whereas the *Actinomyces bovis* (Boström), for example, will grow on gelatin, which it slowly liquefies even at 15° C., and is distinctly an aerobic form, though it is also a facultative anaerobe

Some varieties of actinomyces appear to carry on a saprophytic existence outside the body on the awns of barley and on other graminaceæ, and thus infect the mouths of animals which eat them. Infection may also be conveyed through wounds and accidental scratches.

In recent years different varieties of streptothrix have been isolated in pure culture from a considerable number of cases of clinical actinomycosis both in man (Foulerton and Price-Jones, and more recently Colebrook) and in a number of the lower animals. They have been investigated more especially by Nocard, and the whole group may be spoken of as Nocardiaceæ.

Mycetoma (Streptothrix maduræ, Madura foot).—Madura disease is somewhat closely allied to actinomycosis both in the general characters of its naked-eye appearance and in the presence of the fungus in the form of visible granules in the pus and degenerated tissues of the lesions The pathological changes which occur are due to an organism met with in two varieties, the one producing yellowish granules, the other black ones. The form producing yellow granules is a streptothrix; the black variety is said by J. H. Wright to be a

hyphomycete, and is a good deal rarer than the yellow form. Mixed infection with the two varieties may be met with.

In the pale (yellow) variety the granules exhibit on examination a mycelial network similar to that observed in actinomycosis, and may present some degree of clubbing at the ends of the threads.

The organism has been grown on gelatin and on agar, and is aerobic. It forms rounded and elevated but *flattened yellow colonies, which* upon agar may assume a reddish tinge. It does not liquefy gelatin. It grows more freely than the actinomyces, and can be cultivated down to 6° or 8° C.; its optimum is about 37° C. It is Gram-positive.

The black variety grows well on ordinary media, forming a thick mycelial network upon which black granules may appear as the culture gets old. It is Gram-positive.

In the case of both varieties, animal inoculation has given negative results.

Spironema pallidum (Spirochæte pallida, Treponema pallidum).—This organism (Plate 8, Fig. 4) was discovered in 1905 by Schaudinn in the mucous patches in a case of secondary syphilis. It differs from other spirochætes, which are normally present in the mouth and about the external openings of the genital organs, in being *much thinner and extremely pallid and translucent. It is only seen* with difficulty in unstained preparations unless a "dark-ground" illumination be employed, since its refractive index is apparently almost identical with that of the material in which it is found.

Schaudinn and Hoffmann (1905), continuing the investigation of the organism, proved its invariable presence both in the primary lesion of syphilis and in its secondary eruptions. Shortly afterwards it was found both in the blood and in the internal organs in secondary syphilis as well as in the tertiary lesions, and also in cases of the congenital affection. It has also been identified in syphilitic lesions of the brain and spinal cord.

A further evidence of the specificity of the organism was afforded by the experiments of Metchnikoff and others on the production of syphilis by the inoculation of syphilitic material in anthropoid apes. In these cases the spironema was always found to be present in the lesions which resulted from the inoculations.

Although it has not hitherto been possible to cultivate the spiro-*nema on ordinary artificial media*, Noguchi has succeeded in growing it on a special medium, and has produced the disease experimentally by the inoculation of pure cultures. There is thus no longer any question but *that it is undoubtedly the specific causal agent* of syphilis.

The micro-organism is a screw-shaped body with sharp turns, bent like a corkscrew whose successive coils are closely set together. The two extremities tend to be *straightened out and somewhat pointed.*

Measured in a straight line, it covers a length of 4–15 μ, and the width of the thread is 0·1–0·2 μ. The number of coils exhibited may vary greatly, and may be as few as 5 or 6, or as many as 20 or more.

When examined in fresh syphilitic material the organism is seen to be very actively motile, and movements of rotation round the long axis, flexion in its length, and alternating advance and retrogression take place rapidly. The screw shape is maintained throughout these movements.

The spironema is difficult to stain by the ordinary methods employed for bacteria, but stains quite readily by Romanowsky's, by Leishman's, or by Giemsa's method (p. 43), after the tissue or the film of fresh material has been fixed in absolute alcohol.

In fresh syphilitic material the organism is readily demonstrated by Burri's indian-ink method. Some of the suspected matter is emulsified in a little water, and a minute quantity is taken up with a fine drawing-pen, which is then dipped into a series of tiny drops of indian ink upon a slide one after another, as if making dilutions. The drops are allowed to dry, and examined without cover-glass with the oil-immersion lens. The spironema stands out brilliantly white upon the grey-black background.

In cases of suspected syphilis in which the attempt to discover typical spironemas in the lesions proves unsuccessful, the diagnosis may be obtained by employing the Wassermann or Dreyer-Ward syphilis reaction (pp. 53, 56).

Ducrey's bacillus (bacillus of soft sore).—This organism was described by Ducrey, in 1889, as occurring constantly in ulcus molle, and he showed that by a series of inoculations of the skin—the first of which was made from the pus of a soft sore, the second from the lesion caused by the first inoculation, and so on—he could succeed in obtaining a pure culture of the organism in a sore having the typical appearances of an ulcus molle.

Ducrey's results were shortly afterwards confirmed by Krefting, who found the bacillus in a series of 13 cases of soft chancre, as well as by a number of later observers. Krefting also showed that the bacillus may be present in pure culture in the buboes which frequently accompany the condition.

The organism has not been found in any other ulcerative condition of the skin, and no other organism has been found with constancy in buboes associated with soft chancre. Ducrey's bacillus is therefore generally accepted at the present time as the probable specific causal agent of this affection.

It is a short, rod-shaped organism, very similar in appearance to the *Bacillus pestis*, measuring about 1·5 μ long, and 0·5 μ wide. It is not motile, and has no flagella. It does not form spores.

cases all of these procedures should be adopted with bacterial remedies. Oral and rectal administration of serums and vaccines have both been advocated from time to time, but although some value has been claimed for these methods they are probably useless so far as specific results are concerned. At the same time, it is only fair to point out that the immunity towards the typhoid bacillus acquired, for example, by the soldier in India is an instance of the efficacy of an unsensitized vaccine unwittingly administered by the mouth. Serums should be injected subcutaneously, intramuscularly, intravenously, or intraspinally, according to the severity or other circumstances of the individual case. Vaccines should be injected subcutaneously.

The syringe.—The *serum syringe* should be of a capacity of not less than 10 c.c., and should be of the all-glass variety, as this can be readily and effectually sterilized (Fig. 2). The needle should be somewhat longer than that of a common hypodermic syringe; 5 or 6 cm. is an adequate length. The bore of the needle need not be

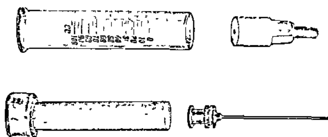


Fig. 2.—All-glass serum syringe; readily sterilized by boiling after separation of the component parts.

large, as the serum is perfectly fluid and will pass readily through any hollow needle, and it is an advantage rather than otherwise to give the injection slowly.

The component parts of the syringe—the barrel, piston, nozzle, and needle—should be separated and boiled just before use, to ensure sterility. After fitting up, the syringe must be allowed to cool before the serum is drawn into it, to avoid any coagulation of the albumin. Immediately after use the needle should be disconnected, the syringe dismantled, and its component parts thoroughly washed through with cold water before again being sterilized.

The *vaccine syringe* should also be "all glass," of 1 c.c. capacity, graduated in tenths or twentieths of a cubic centimetre, and provided with a short fine needle; if provided with a coloured piston—e.g. blue or brown glass—the recognition of the quantity of fluid in the syringe is facilitated. It should be sterilized for use in the same way as the serum syringe.

1. Subcutaneous injection. *Site.*—Premising that the serum or vaccine should be introduced into loose, subcutaneous tissue, the exact spot selected is of little importance so far as the ultimate result is concerned, although the sides of the abdomen, towards the loin or near the groin, and the back, between the shoulders, and in females the loose tissue at the base of the mamma, are favourite spots. Certain considerations, however, influence our choice. In the first place, a small lump is frequently noted at the seat of inoculation, which persists for a day or two, or perhaps longer, often associated with some tenderness, hence a locality should be selected which is subject to little movement, and is not pressed upon by the patient's clothing or during work or sleep, or subjected to friction. Therefore, in the male, parts subjected to the pressure of braces, and in the female, of corset bones or laces, should be avoided. If a second injection is required, it may be given at a point corresponding with the first, but at the opposite side of the body; if a series of doses is necessary, rows of punctures may be made in lines up the two sides of the body.

In both sexes the forearm, where the subcutaneous tissue is small in amount and constant friction is experienced between the skin and the muscle beneath, is a particularly bad locality for the injection of vaccines, although its ready accessibility renders it extremely tempting for this purpose.

Preparation.—Wash the selected site thoroughly with ether soap on a piece of lint, pour ether on to the area to wash away the soap, and finally cover with a piece of sterile lint saturated with ether the spot it is proposed to puncture.

Injection.—Pinch up a fold of the prepared skin between the thumb and forefinger of the left hand, with a quick movement pass the needle through the skin into the subcutaneous tissue, and inject the fluid slowly. When the dose has been administered, withdraw the needle, and if the volume of fluid that has been injected is large, seal the puncture with a layer of collodion or a small disc of adhesive plaster.

In infants the small size of the parts must be borne in mind, and the needle inserted carefully and not too deeply.

2. Intravenous.—The vein usually chosen is either the median basilic or median cephalic at the bend of the elbow; sometimes one is driven by circumstances to select a superficial vein of the forearm or hand, or else of the leg The preparation of the patient is generally quite a simple matter, especially when one is able to attack a vein at the bend of the elbow, for in this situation the skin is delicate, hairless, and easily cleansed The patient should be lying in bed or reclining on a couch. The arm, bared to the shoulder, should rest on a clean towel on the bed by the patient's side, or, better still, drawn out at right angles to the body, and the skin thoroughly washed with soap

and water. Then the skin over the selected vein is scrubbed with ether, more ether is poured on and allowed to evaporate, and finally the site for operation is covered with a piece of lint saturated with ether. If some other vein, possibly covered by hairy skin, is chosen, the part must be washed up with ether soap, carefully shaved, the skin scrubbed with lysol, and then the lysol thoroughly washed off with large volumes of ether, the skin being finally covered with a pad saturated with ether. Now a tourniquet or a bandage is applied tightly round the upper arm, to retard the venous return (but not so tightly as to interfere with the arterial flow), and so cause the vein to become distended and prominent.

Next open the phial containing the antiserum and fill the previously sterilized all-glass syringe with serum. The ether pad is now removed from the patient's arm, and after waiting for a few moments to allow the last trace of ether to evaporate, the point of the needle is plunged through the skin by the side of the vein, then its direction is slightly altered and it is pushed on so that it enters the vein obliquely. The blood in the vein, being under pressure owing to the application of the bandage above, enters the syringe, and the moment it appears in the barrel of the syringe the tourniquet is removed from the arm and the serum slowly and steadily injected into the vein. The patient's blood, being heavier than the serum, sinks down into the barrel of the syringe immediately beyond the nozzle, and practically the whole of the serum contained in the syringe can be delivered into the vein without returning the blood which first appeared in the barrel.

3. **Intraspinal.**—Two sterile syringes are required, each of which will fit on to the same needle, which should be of stout rigid steel, 6–7 cm. long for children, and 9 cm. for adults. One syringe should be filled with serum and covered with an inverted glass dish to prevent contamination. The other syringe, with the needle attached, is used for the actual lumbar puncture.

Arrange the patient in bed in the semi-prone position, on whichever side is more convenient to the operator. Raise the head slightly on a pillow. Bend the knees and flex the thighs on the abdomen so that the vertebral column is well arched, and hold the patient firmly in this position. The site of operation for lumbar puncture is a 10-cm. (4 inches) circle of the skin of the back, having its centre over the spinous process of the fourth lumbar vertebra. This central point can be identified by the simple method of counting the vertebræ downwards, or by the help of a line joining the highest points of the iliac crests—which crosses the fourth lumbar vertebra. Adjust either the bed or the light so that the field of operation is well lighted The skin over the area already indicated is prepared as was the bend of the elbow for the intravenous injection. The needle is introduced

into the interspace between the third and fourth lumbar vertebræ and pushed on between the laminæ into the spinal canal, and at least 10 c.c. of fluid collected in the syringe. As a general rule, rather more fluid should be removed than it is intended to replace by serum. Indeed, when the intraspinal pressure is much increased it frequently happens that the bulk of fluid withdrawn is much in excess of the volume of serum it would be safe to introduce into the spinal canal. The syringe is now detached from the needle and put on one side, while the syringe full of serum is adjusted to the needle already *in situ* and the serum slowly injected.

ANTITOXIC SERUMS

Diphtheria.—Antidiphtheria serum is standardized experimentally according to the number of units of antitoxin contained in each cubic centimetre of the serum, the unit of antitoxin being that smallest quantity which, when mixed with 100 lethal doses of diphtheria toxin and injected into a guinea-pig, will prevent the appearance of any toxic symptoms; a combination occurring in the animal's tissues between the toxin and antitoxin in such a way that the poisonous effects of the former are completely neutralized. The same phenomenon obtains in the human body, but as it is impossible to estimate the amount of toxin that has already gained access to the tissues in the patient infected naturally, it follows that one must be prepared to use a large excess of antitoxin in order to neutralize not only the poison already formed, but also that which is in process of formation by the living diphtheria bacilli remaining in the throat; for the effect of the serum being antitoxic only, it does not act directly injuriously upon the infecting organisms. According to the authors of the previous article, in using antitoxin as a prophylactic agent in diphtheria, from 2,000 to 4,000 units should be administered in a single dose, while, as a therapeutic dose, in severe cases several times this amount may have to be given, and the dose repeated at frequent intervals until definite improvement begins to take place. I agree with them that there is still a tendency, as in the case of tetanus antitoxin, to administer the remedy in insufficient amounts, so far as concerns its therapeutic use, but as a prophylactic agent it will generally be found, in my opinion, that 500 or 1,000 units need rarely be exceeded.

Tetanus.—Tetanus antitoxin may be used either prophylactically or therapeutically. In the former case, preventive inoculations should always be used in cases of crushed and lacerated wounds into which garden soil or road dust has been carried at the time of injury. Its therapeutic use is sufficiently discussed in the article on Tetanus (page 930), and it need only be added

that the remedy cannot be said to have had a proper trial in a case of tetanus unless it has been administered promptly, repeatedly, and freely in large doses, by all the available routes, viz. intraspinally, intravenously, intramuscularly, and subcutaneously as well as locally. To say that doses of 100 or 200 units of antitoxin should be repeated as often as the case allows, until some definite result has been obtained, might appear to suggest heroic treatment, but it must always be remembered that the mortality of acute tetanus is in any case extremely high, and in many statistics reaches even 80 per cent.; moreover, clinical symptoms of the disease do not become manifest until the infection has attained serious proportions.

ANTIBACTERIAL SERUMS

Streptococcic infections.—In surgical infections due to the *Streptococcus pyogenes,* especially those of the septicæmic type, treatment with antistreptococcic serum possesses considerable value, especially if the serum employed is *polyvalent;* that is to say, serum obtained from an animal immunized by the injection of a large number *of strains of streptococci derived from various sources and types* of infection. Streptococci derived from different sources vary widely in their behaviour towards an immune serum prepared from one particular strain, although, so far as concerns cultural characters, the streptococci themselves may be identical. Hence the use of a polyvalent serum affords the hope that it may contain specific antibodies for a strain that is sufficiently closely allied to that which is infecting the patient. The best results are obtained by injecting large doses at once, 20–30 c.c., either intravenously, or half intravenously and the remainder subcutaneously. In favourable cases the temperature will undergo a marked fall in 6–12 hours, and a further dose of 10 c.c. administered 36–48 hours after the first may be all that is needed, but any subsequent considerable rises of temperature indicate the necessity for the injection of more serum. If the first injection fails to lower the temperature appreciably within 24 hours, a supply of serum *prepared by a different firm of manufacturers* should be procured and injected (Chart 1), and in the event of its failure to influence the course of the infection other brands of serum may be tried in turn, if the opportunity still exists. But by the time the third dose of serum is due, the particular strain of streptococcus responsible for the infection will, or should, be available in pure cultivation, in which case it is preferable to select the serum to be used for the treatment of the patient by testing all the procurable brands of serum against the patient's own streptococcus and employing the one that has the highest antibody (immune body, agglutinin, etc.) content. At this

stage, too, treatment with an autogenous vaccine may be substituted for or combined with the serum treatment.

Another plan which has occasionally given excellent results in the writer's hands consists in the immunization of a human donor with a vaccine of the streptococcus isolated from the patient. In the healthy subject, antibody-formation proceeds fairly rapidly, and after a few injections, extending over perhaps 10 days or a fortnight, immune body can be demonstrated in the serum in fair quantity, and at this stage either whole-blood transfusion can be carried out or the donor

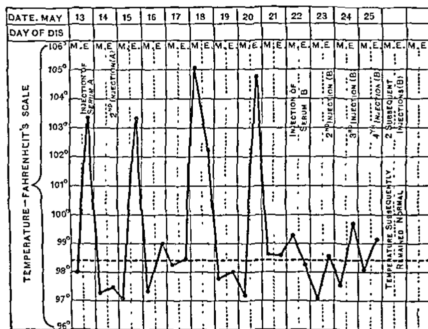


Chart 1.—Illustrating the efficacy of a second brand of anti-streptococcic serum after failure of the first.

can be bled, the serum separated and injected into the patient. Unfortunately, the course of a streptococcic infection as a rule is too rapid to allow the time necessary for the immunization of the donor.

Anthrax. — The antiserums prepared by Sclavo and by Mendez have been found to possess very great therapeutic powers, and in Italy in unoperated cases treated with serum the mortality has been reduced from 24 per cent. to 6 per cent in the human subject. Serum may, therefore, be used as an alternative to operative procedures, although unless the serum is ready to hand when the case is first seen very few surgeons would care to run the risks inseparable from delay. The dose of serum is 20–40 c.c, and should be injected intravenously.

or half intravenously and the remainder subcutaneously into the flank. From the curative point of view, one dose is usually sufficient.

VACCINE TREATMENT

Bacterial vaccines and their preparation.—The vaccine used in any given case may be one of two kinds—either "autogenous," that is to say, prepared from the actual organism isolated from the patient; or "stock," that is, prepared from a cultivation of the same species of bacterium already isolated and stored in the laboratory.

Either type of vaccine may be "sensitized"—that is to say, combined with its own specific immune body, so that the mixture only needs the addition of complement to ensure its rapid disintegration, and this is already present in the body of the individual to be inoculated. Finally, a sensitized vaccine may be prepared with the micro-organisms in the living state or killed by heat.

Vaccines detoxicated by a preliminary digestion with alkalis and acids have been recommended by various observers. Their mode of action, however, appears to be similar to that of solutions of peptone, and probably comes under the heading of "protein shock," since experiments upon animals in my laboratory and the investigation of serum from patients in the vaccine department suggest that *specific* antibodies *are not formed as the result of their use.* In this respect they are, in my opinion, inferior to the various types of vaccines already referred to.

Detoxication in the sense that the power of toxin-formation has been diminished or abolished by prolonged laboratory culture under carefully adjusted conditions has only been attained in a few bacteria—notably *B. anthracis,* the attenuated culture (Pasteur) of which has proved of great value in veterinary work, and *B. tuberculosis,* of which a bacillary emulsion (Raw) is likely to prove equally valuable in human therapy. So far as autogenous vaccines are concerned, however, this class of detoxicated vaccine is at present outside the range of practical therapy.

A stock vaccine may be prepared from one "strain" or type of micro-organism, or by first mixing together a number of cultivations representing many strains of the same species; in the latter case *the vaccine is spoken of as a* "*polyvalent*" or "multivalent" stock vaccine. For prophylactic use a stock vaccine must necessarily be employed. For therapeutic administration each variety of vaccine has its own sphere of usefulness, but, speaking generally, a polyvalent stock vaccine is *inferior in value to an autogenous vaccine,* and a stock vaccine prepared from a single strain is still less valuable

than one prepared by mixing several strains. Occasionally it happens that, although the diagnosis has been accurately made, it is found to be impossible to isolate the actual infecting microbe in the *pure* culture necessary for the preparation of an autogenous vaccine, in which case the use of a polyvalent stock vaccine is indicated. Or, owing to the admixture of the infecting organism with other and adventitious bacteria, there may be considerable delay in separating out the responsible microbe; here, again, one may be compelled to employ a stock vaccine to tide over the interval before the autogenous vaccine is completed.

No matter what variety of vaccine is employed, the method of preparation is the same. The required organism, freshly isolated from the human subject, or recently passed through the body of a laboratory animal, is cultivated upon a suitable medium—usually agar or blood-agar—under such conditions of time, temperature, etc., as experience shows will give the largest number of living virile individuals. The resulting bacterial growth is scraped from the surface of the medium and emulsified in a test-tube with a 0 1-per-cent. solution of sodium chloride; some glass beads are added, and the emulsion thoroughly agitated in an electrical or other form of mechanical shaker, in order to secure a perfectly homogeneous suspension. The number of bacteria present in a unit volume of the emulsion is then ascertained. This can be done by means of one or other of the recognized methods, such as plate-culture "counts," decimal dilutions, Thoma-Zeiss or other counting-chamber, comparison with a standard emulsion or with normal blood; or, as so many of the pathogenetic bacteria have been weighed and the weights recorded for reference, by drying and weighing. The use of opacity methods, in which the personal equation bulks much too largely, is not advised. The most generally convenient method is undoubtedly Wright's, which consists in mixing equal quantities of the emulsion and the blood from a normal subject, spreading the mixture in a thin film on a slide, staining with Leishman's or Jenner's stain, and, with the help of the microscope, estimating the ratio existing between the red cells and the bacteria in the preparation. Now, assuming 5,000 millions of red cells per cubic centimetre as a constant for normal blood, the number of germs per cubic centimetre of emulsion is easily calculated.

The emulsion is next sterilized by exposure in a water bath for one hour to that temperature (usually between 55° C. and 60° C.) which is known to destroy the bacterium concerned in that time with the least possible alteration in the constitution of its protoplasm, and the sterility of this "killed culture" is controlled by attempts to sub-cultivate portions of it in or upon other media.

Sensitization, if desired, is effected at this stage (or in some cases prior to sterilization, according to whether a dead or a living sensitized vaccine is being made) by mixing the bacteria with the serum containing their appropriate antibody and allowing the mixture to stand in the cold for 12 hours. All traces of serum are then removed from the bodies of the bacteria by successive washings in normal saline solution

The next step is to dilute the emulsion with some weak, non-irritating, antiseptic solution[1] (with a view to preventing subsequent contamination) so that each cubic centimetre shall contain a standard number of germs—e g. 1,000 millions or 100 millions—as from such an emulsion various doses of the vaccine containing smaller numbers of bacteria can readily be measured for injection into the patient. Finally, the vaccine is either preserved for use in bulk in rubber-capped bottles, from which the necessary dose can be taken as required, or separate doses are measured out and each put up in a small glass ampoule, the neck of which is subsequently sealed in the blow-pipe flame. The former is more convenient when a large quantity of stock vaccine is needed for immediate use, as in prophylactic work, but the latter is preferable when the vaccine is required for the treatment of the individual patient over a period of weeks or longer.

The above method is modified somewhat in the case of vaccines prepared from the tubercle bacillus. In the first place, the slow growth of this organism necessitates the use of cultures which have been incubated for several weeks. One form of vaccine, known as bacillary emulsion (B E.), is prepared by scraping the growth of the tubercle bacillus from the culture medium, drying the mass *in vacuo*, and then triturating in a mortar and emulsifying the powder in a 50-per-cent. aqueous solution of glycerine. After allowing the heavy particles to deposit, the supernatant opalescent fluid is pipetted off and standardized by dilution to contain the equivalent of 5 mg. of dried tubercle bacilli per cubic centimetre. Another tubercle vaccine, known as Koch's New Tuberculin (or T.R.), is prepared by first washing the dried and powdered tubercle bacilli with distilled water and then centrifugalizing. The supernatant opalescent fluid is removed, and the residue, now freed from soluble toxins, dried, and the process of extracting by triturating with 20-per-cent. glycerine solution (in the proportion of 10 mg. of dried powder to 1 c.c. of glycerine solution) is then repeated several times, the fluid used each time being preserved and the whole finally mixed together. The dosage of tubercle vaccines is usually calculated in fractions of 1 mg. of the dried tubercle bacilli.

[1] Those in general use are phenol 0·5 per cent., lysol 0·25 per cent., and trikresol 0·25 per cent.

Active immunization by vaccines.—The hypothesis upon which vaccine treatment was originally based assumes that certain substances—opsonins—existing in the blood-serum have the power of so sensitizing bacteria that gain entrance to the tissues as to render them readily ingested and destroyed by the phagocytes, and it is to the presence of these substances that the natural resistance of the individual is due If the number of bacteria invading the tissues is small and the available amount of opsonin adequate, no infection—in the clinical sense of the term—results. If, however, the available opsonin is inadequate to sensitize all the bacteria, and some escape destruction by the phagocytes, infection takes place. The stimulus provided by the action of the surviving bacteria should provoke the formation of specific opsonin adequate in amount to ensure the destruction of the bacteria, and so terminate the infection; failure in this direction is followed by the rapid multiplication of the germs, and the resulting train of clinical symptoms, which provide the oppor-

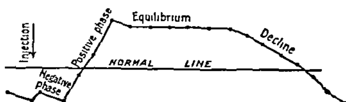


Fig. 3.—The opsonic cycle.

tunity and necessity for vaccine treatment. In all probability this hypothesis takes cognizance of one only of many factors concerned, and that perhaps a quite insignificant one, but, because of the ease with which this particular factor can be identified and observed throughout the course of an infection, the hypothesis is a practical and convenient one to work with, as will be seen if we trace the effect of an injection of vaccine upon the opsonin content of the patient's serum.

The immediate result of the introduction of a dose of vaccine into *the tissues of a patient is a fall in the amount of opsonin present in* the serum, owing presumably to the linking-up of some of the available opsonin to the bodies of the bacteria introduced. This is termed the "negative phase," and occupies a period lasting from a few hours to a week or 10 days, or in exceptional cases a fortnight or more. Its duration is increased by a larger dose, and reduced, or even eliminated altogether, by a smaller dose. During this period, although no appreciable rise of temperature occurs which can be directly attributed to the injection of the vaccine (unless an excessive dose has been administered), the patient sometimes complains of not feeling

well, and any local lesion that may be present is objectively worse—the discharge from a sinus increases in amount; in a cystitis there is an increase in frequency of micturition, and more pus is present in the urine; in furunculosis a fresh crop of boils may appear, and so on.

As a result of the stimulus provided by the vaccine, fresh supplies of opsonin are elaborated and discharged into the serum, and the negative phase is succeeded by a positive phase, during which the opsonin index rises slowly or rapidly to a maximum, a subjective sense of well-being is experienced, pyrexia diminishes, often rapidly, and clinically the improvement is marked. After reaching the maximum, the index frequently oscillates slightly for a day or two, and then comes to rest, and a condition of equilibrium is established, in which the index is maintained at a higher level than it occupied before the injection, although even now not necessarily at or above the normal. This state of equilibrium, after a period varying with different individuals, with the size of the dose, etc., declines either gradually or rapidly until it has fallen to, or below, its original position. A repetition of the dose of vaccine now causes a repetition in their entirety of the phenomena already detailed. This opsonic cycle is graphically represented by the curve in Fig. 3. If, however, a second dose of vaccine is administered during the negative phase induced by the first injection, a cumulative action is noted, and a second

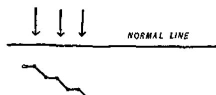


Fig. 4.—Opsonic index, showing rapid fall.

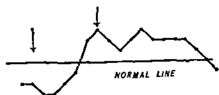


Fig. 5.—Opsonic index, showing less marked negative phase.

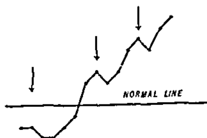


Fig. 6.—Opsonic index, showing cumulation of positive phases.

negative phase is superposed on the first; the opsonic index will then rapidly fall, perhaps with serious results to the patient (Fig. 4). On the other hand, a second dose injected at the highest point of the positive phase will not in most instances give rise to cumulation of

positive phases. Usually such a procedure merely results in a shorter or less marked negative phase (Fig. 5); but in some infections, e.g. those due to the gonococcus and the *Bacillus coli*, that highly desirable end can be obtained (Fig. 6) Practically it is found that good clinical results are obtained if the index oscillates about the normal level, provided that the greater part of the curve representing the movements of the index is above normal (Fig. 7). Consequently, to obtain the best results by the aid of vaccines, subsequent doses should be injected towards the end of the period of equilibrium. Endeavour should be made so to adjust the dose as to obtain the shortest negative

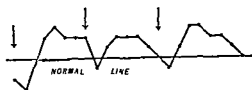


Fig. 7.—Opsonic index, showing oscillation about normal level.

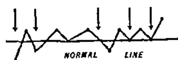


Fig. 8.—Opsonic index, showing immediate appearance of positive phase.

phase compatible with the production of a positive phase lasting for five to seven or more days.

In many acute infections, however, it is of greater importance to reduce or eliminate the negative phase which follows the injections than to lengthen the positive phase, and in such cases a dose must be administered so minute that the positive phase appears almost immediately, and must be repeated before the transient positive phase has declined, sometimes within twelve hours (Fig. 8).

General considerations.—Practically every case of bacterial infection presents points of peculiarity, and, although it is impossible to lay down any hard-and-fast rule for treatment by vaccines, a few general considerations can be stated as the result of experience accumulated by many workers during the last few years.

1. It is absolutely essential that the diagnosis should be accurate, and that full and complete information should be available as to the exact organism responsible for the infection.

2. The estimation of the antibody content of the serum is not absolutely essential to the successful conduct of treatment, careful attention to the general clinical features of the case being in most instances sufficient guide for the administration of vaccine in the acuter forms of bacterial infection. In the subacute and chronic types the weighing machine will be found a useful adjunct to clinical observation.

3. The reactions directly consequent upon injections of vaccine

may be grouped under the headings of local, focal, and general. *Local* reaction is almost always the rule when injections are made into the arm or leg—elsewhere it should be conspicuous by its absence; if it does occur it should be insignificant and transient, limited to slight swelling and erythema at the seat of the inoculation with tenderness on pressure, all passing off within twenty-four hours. More "reaction" than this raises a suspicion of lack of skill, neglect of antiseptic precautions, or contamination of the vaccine. Local rashes, dermatitis, and eczema are usually due to the action of the antiseptic employed for cleansing before inoculation upon a sensitive skin. In exceptional cases, as for example where large doses of tubercle bacillary emulsion are employed for chronic cases, local necrosis sometimes occurs, followed by softening, and ultimately by the evacuation of a sterile grumous fluid *Focal* reaction affords the most satisfactory guide to dosage and interval, and the objective signs that accompany the negative phase have already been referred to in that connexion (p. 122). This exacerbation of the main feature of the infection usually becomes apparent in 6–12 hours after the administration of an appropriate dose of vaccine; a reversion to the antecedent state occurs in about 24 hours; then distinct improvement manifests itself in 36–48 hours.

General constitutional reaction in its most marked form should be limited to malaise, headache, languor, or drowsiness, of a very slight and transient character, passing off within 24–48 hours. Pyrexia, when directly attributable to the vaccine and not a mere coincidence, indicates too large a dose. Under this heading must be mentioned the urticaria which sometimes appears during the treatment of intestinal infections by vaccines prepared from intestinal streptococci or some members of the *B. coli* group.

4 When undertaking vaccine treatment without the assistance of the serum estimations, it is essential to employ small initial doses, in order to avoid the risk of a negative phase excessive in amount or duration. Then, too, the age, weight, and general condition of the patient must to a certain extent be taken into consideration. Speaking generally, an emaciated infant would receive a very much smaller dose than a well-developed and apparently vigorous adult. With acute and generalized infections the initial dose should be very small indeed, perhaps not more than one million bacteria, but in subacute infections it may well be ten times as large, and in chronic conditions a hundred times as large. Again, so long as improvement is maintained with any given dose, it may be stated in general terms that there is no object in increasing that dose. With most vaccines, however, it will be found that after a time any given dose is incapable of provoking a response equal to that at first obtained

and then it is necessary to increase the dose; but with tuberculin it may be unnecessary to alter the dose from that originally determined, throughout the whole course of treatment.

5. It should be remembered that a dose sufficiently large to provoke marked constitutional disturbance and pyrexia usually goes hand in hand with a negative phase of considerable extent, and should be an indication for making the ensuing dose very much smaller in size.

6. Surgical treatment, carefully conducted, should accompany the vaccine treatment throughout. Thus, whenever possible, an infected area should be immobilized, an infective focus removed, and so on.

With these few general considerations we may pass at once to some slightly fuller details for the treatment by vaccines of infections by the various micro-organisms which more commonly come under the cognizance of the surgeon, arranged under the headings of the infecting organism.

Staphylococcus pyogenes aureus, albus, and citreus. —Of the infections due to either of these organisms, suppuration is usually the main manifestation of the pathogenetic activity of the cocci; but the lesions that the surgeon may desire to treat by vaccines include not only pustular acne, furunculosis, boils and abscesses, but also the more diffuse suppuration of osteo-myelitis, and staphylococcic septicæmia. In either of these lesions, the albus, citreus, or aureus staphylococcus may be present alone or in combination; the necessity for accurate diagnosis therefore is obvious, for, contrary to some recorded opinions, a vaccine of one of these staphylococci is inadequate for the treatment of an infection due to either of the others.

Polyvalent stock vaccines of the *S. aureus* appear to be fairly effective in localized infections, but are of little value when the infection has become generalized. Stock vaccines of the *S. albus* are of considerably less value, and whenever it is possible to avoid doing so should not be allowed to replace autogenous vaccines. Neglect of this point has no doubt led to many of the failures in the treatment of pustular acne—an infection frequently due to the *S albus*—stock vaccines of the *S. albus*, or even of the *S. aureus*, having been used in place of an autogenous vaccine.

For the preparation of autogenous staphylococcic vaccines the organism should be grown upon nutrient agar (pH = 7) for 24 hours, at a temperature of 37° C. Emulsion should be killed by exposure in the water bath to a temperature of 60° C. for one hour.

The size of dose usually employed varies with the severity of the infection. A staphylococcic septicæmia would not, at any rate in the early stages, receive a larger dose than 10 to 25 millions, while the subacute and chronic suppurations due to these organisms will usually

other chronic inflammatory states, but are frequently more difficult to cure owing to environment and local conditions.

"2. Chronic cases, where the gonococcus is the sole infecting organism, have a better prognosis from the point of view of treatment by vaccine than a mixed infection or one of staphylococcus only.

"*III. Chronic gonorrhœa with complications.*—1. Chronic gonococcus infections present clinical features which themselves afford valuable indications during the course of vaccine treatment.

"2. Where the gonococcus alone is the infecting organism, routine injections of from 1 million to 2 million cocci every three to five days are safe and satisfactory; a lapse of five *to seven days after doses* of 5 millions; an interval of eight to ten days after inoculation of 10 millions. Larger doses than these are seldom desirable.

"3. Treatment by small and gradually increasing doses at frequent intervals should at all times be observed; the use of large doses is even more dangerous than in acute cases, and may be followed by disastrous consequences.

"4. In *orchitis, small doses of vaccine quickly relieve pain and* cause a more rapid abatement of symptoms than is obtained by the usual routine treatment alone.

"5. In iritis the severe pain, which is a marked and obstinate feature, is relieved in 48 hours after an injection, and disappears in from three to four days; cure is much hastened.

"6. In arthritis the treatment is of considerable value."

Micrococcus catarrhalis.—*Under this term is included a* group of closely allied cocci most usually met with in catarrhal conditions of the mucous membrane of the nose and throat. Surgically, *M. catarrhalis* is found sometimes as the sole responsible organism in pyorrhœa alveolaris, sometimes associated with either the *Streptococcus pyogenes* or the *Diplococcus pneumoniæ*, or with both. Vaccines of this organism should always be autogenous. The coccus should be grown *on nutrient agar at* 37° C. *for* 24 hours, and killed by exposure to 57° C. for one hour. As the toxicity varies considerably with the different strains, it is always well to commence with small (5-million) doses at intervals of four or five days, gradually raising the dose to 50 or even 100 millions as the patient responds to the injections. With the larger doses, intervals of eight to ten days are advisable. In the treatment of pyorrhœa, local treatment, i.e. scaling, and *dressing of the pockets* round the teeth, should be carried on side by side with vaccine treatment As many patients show a very pronounced negative phase if the hypodermic inoculation of the vaccine is administered within a short time of the mechanical treatment of the mouth, an injection should not be given within a couple of days of local treatment.

Bacillus coli communis.—The surgical conditions in which this organism is met with include appendicitis, peritonitis, cystitis, pyelitis, colitis, and ischio-rectal abscess, as well as other localized suppurative processes Stock vaccines of *B. coli* are practically worthless. In the preparation of autogenous vaccines the organism should be grown on nutrient agar at 37° C. for 24 hours, and killed by exposure to 58° C. for one hour. In acute conditions due to *B. coli*, 2½ millions may be all that the patient can stand. Usually, doses of 5 millions can be given at intervals of four or five days, proceeding to doses of 10 millions at intervals of about a week. Finally, doses of 50 millions can be given, sometimes at weekly and sometimes at fortnightly intervals, according to the resistance of the patient, the clinical symptoms in coli infections forming a very reliable guide. The nausea and anorexia, together with the rise in temperature in pyrexial cases, which mark the negative phase, should not exceed 24 hours in duration, and the size of the dose or the interval between the doses should be so regulated that a short negative phase is obtained. Prophylactic injections of vaccines of the colon bacillus prepared from the patient's alimentary canal are of distinct value as a routine preparation for appendix operations other than those of emergency.

B. pyocyaneus.—This organism is frequently met with as the causative agent in abscess-formation, in ulcerative colitis and otitis, and is also commonly concerned in suppuration following extensive burns and scalds. The vaccine should be prepared in a similar manner to that mentioned for B. coli, and the injections should be given at intervals of five or six days, commencing with doses of 50 millions, and rising gradually to doses of 100 or 200 millions.

Bacillus pneumoniæ is met with in abscesses, especially those in the neighbourhood of the kidney, in cystitis, and in empyemas, also in localized abscesses in other situations. The initial dose of this organism is 5 to 10 millions, rising to doses of 100 millions, the intervals being usually six or seven days.

Bacillus mallei.—The vaccine treatment of acute glanders is by no means successful. Subacute and chronic cases may appear for a time to do well, but similar improvement in the clinical condition of these patients has been observed under any form of treatment, and, so far as one can see, the final results are the same. The employment of vaccines in these conditions is, therefore, not advocated.

Bacillus tuberculosis.—In the various forms of localized tuberculosis the use of vaccine (tuberculin) prepared from this organism is of the utmost value. Many cases—joints, bones, epididymis, kidney, etc—that would formerly have been operated upon the moment the condition was recognized, will in favourable circumstances undergo complete cure with the use of tuberculin alone;

although, where the tuberculous process is well advanced before the diagnosis *is made, it is advisable, if in any way possible, to remove* the local focus, in order to shorten the period of treatment. Even when operation is obviously the only satisfactory line of treatment, it is well worth trying to attain even a slight increment in the defensive powers of the patient by tuberculin injections prior to operation. That such a procedure is attended with some measure of success is shown by the rarity of recurrence of, for example, cervical glands after an operation that has been preceded by tuberculin treatment. Care must be taken to exclude phthisis when commencing a course of tuberculin treatment, for my experience has been that patients who suffer from surgical tuberculosis complicated with phthisis require exceedingly small doses of tuberculin, and that usually, while the local lesion rapidly mends, the lung infection either remains stationary or, as more often happens, progresses more rapidly than before. New Tuberculin (T.R.) prepared from human strains of *B. tuberculosis* has given the best results in my hands for all ordinary cases, but Tuberculin (B.E.) is preferred by many workers. In cases complicated with phthisis, tuberculin prepared from bovine sources should be used. Some of these latter do fairly well with Calmette's Tuberculin (CL.). The dose of tuberculin (T R.) varies somewhat with the age of the patient. A small child would receive perhaps 0 0001 or even 0 00005 mg., while a fairly well nourished adult would commence with 0 0002 or 0 0004 mg. The treatment of tuberculosis of the kidney must be started with very small doses, 0 00005 mg, proceeding as the patient improves to 0 0001, 0 0002, and 0 0004 mg. The intervals between doses of tuberculin should not be less than 10–14 days. When a dose of 0 0005 is reached, an interval of 16–18 days will generally meet the case.

Raw's bacillary emulsion (p. 118) can be used in larger doses and at shorter intervals—0 001 mg. gradually increasing to 0 025 mg. at intervals of 7 days; Bovine B.E for pulmonary tuberculosis, and Human B.E. for "surgical" tuberculosis, i e. bones, joints, and glands The weighing-machine affords one of the most important indications as to the correctness or otherwise of the dose and interval. Patients doing well under tuberculin steadily increase in weight, and any error in dosage is promptly followed by a fall in body weight.

Streptothrix actinomyces sometimes seems amenable to treatment with an autogenous vaccine, which should be prepared from 7–10 day-old cultures upon agar, and standardized by drying and weighing Initial doses of 0 001 mg. (which can gradually be increased to doses of 1 mg), at intervals of seven to fourteen days, are of value in combination with operative measures and the oral administration of *potassium iodide.*

INFLAMMATION

By J. M. BEATTIE, M.A., M.D.

There can be no doubt that in the majority of cases the most striking features in an inflamed area are, as will be more fully shown later, the dilatation of the vessels, the slowing or even the complete arrest of the local circulation, the exudation of serum, and the immigration of leucocytes. But, side by side with these changes, the local tissues are reacting in a way which is antagonistic to the agent that has brought about the vascular changes. The connective-tissue and other cells are proliferating, new vessels are being formed, and various changes which have for their object the repair of the damaged area are present in a greater or less degree. It is impossible, in any given inflammatory area, to say where the vascular changes end and the so-called reparative changes begin.

Moreover, in a true inflammatory condition, one or all of the vascular changes may be absent, or may be so slight or so transitory as to be almost negligible. Again, in non-vascular areas, such as the cornea, the degree of irritation may determine the nature of the reaction. There may be only slight proliferation of the corneal corpuscles, or there may be leucocyte emigration, new vessel-formation, etc, and, in fact, all the changes which are seen in a vascular area.

The majority of pathologists now accept the definition of Burdon-Sanderson, that "inflammation is the succession of changes occurring in a part, as the result of injury, provided that that injury be not so excessive as to destroy the vitality of the part." This definition carries us much beyond the view that inflammation is a destructive process. It is a reaction to injury, and has largely for its object the repair of that injury. Destructive processes are always present, and may be in the ascendant; but the reparative processes, too, are never completely absent, and in many cases they are in excess of and more important than the destructive ones.

Thus, strictly speaking, it is not practicable to separate the two processes of *inflammation* and *repair*; but for convenience of study it is advisable to describe the processes as if they were independent of one another, or rather as if repair were a sequel of inflammation.

ACUTE INFLAMMATION

It is important to bear in mind that inflammation is not a disease, but is the result of some noxious influence acting upon the tissues, and that when the cause is removed the process will gradually cease. The heat, redness, pain, and swelling which have always been associated with acute inflammation are easily explained by a study of the changes which take place. The mesentery and the web of the foot of the frog have been largely made use of in experiments on inflammation. Equally convincing results may be obtained by using the omentum of the rabbit or of the guinea-pig (Plate 9). If any of these membranes are exposed under a microscope, a continuous stream of blood can be made out in the capillaries, arteries, and veins; and if a vessel of sufficient size is examined, it will be observed that the blood-stream may be divided into a central yellowish zone, containing the blood-cells, and a clear peripheral or plasmatic zone, containing only an occasional leucocyte Observations on the rate of flow show that in the areas in which the capillaries and venules are dilated, the stream is slower than at other parts. Between the vessels there are fibrous and elastic tissues, as well as nodules of lymphatic tissue.

If an irritant is applied to the membrane, a series of phenomena which are classed under the term "inflammation" is observed. Immediately after the application of the irritant there is a stage of anæmia, in which the arteries are contracted and the blood-flow accelerated. This, however, is only a transitory phenomenon, and is followed by *a dilatation of the vessels, especially of the venules and capillaries*, and a slowing of the blood-stream This slowing may be extremely marked, and at local areas there may be actual arrest of the blood-flow. A change is also observed in the contents of the vessels, for, with the slowing of the stream, the clear plasmatic layer becomes gradually obscured, and *careful examination shows that the leucocytes*, especially the polymorphonuclear variety, have passed from the central to the peripheral clear layer, and are becoming adherent to the lining membrane of the vessels. The part is now red, and considerably swollen, and is seen to be bathed with lymph. The redness is due to the dilatation of the vessels, *and the swelling mainly to the* accumulation of lymph which has exuded from the dilated vessels. More careful observation of the leucocytes will show their amœboid character becoming very pronounced: the pseudopodic processes are pushed against the walls of the minute vessels, and gradually project through them. *The leucocytes become elongated and pear-shaped*, and eventually escape into the surrounding tissues by the minute apertures through which the pseudopodia were first projected



Fig 1.—Acute inflammation in the omentum of a guinea-pig showing a dilated vessel in the centre, filled with leucocytes. Great numbers of emigrated cells are also seen × 200

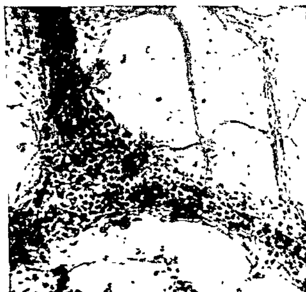


Fig 2.—Acute inflammation in the omentum of a guinea-pig, showing marked emigration of the leucocytes at the junction of tributaries of the vessels. × 200

PLATE 9.

(*From Beattie and Dickson's "General Pathology."*)

(Plate 9, Fig. 1). The transudation of lymph and the emigration of leucocytes become pronounced in a few hours and obscure the picture. For the later changes, portions of the membrane from one animal, or preferably the membrane from different animals, should be removed, fixed, and stained at different periods of time, and in this way the whole series of changes, from the time of application of the irritant to the time when healing is complete, may be examined.

Many of the changes, as has already been indicated, go on side by side, but for convenience of study each may be dealt with in turn.

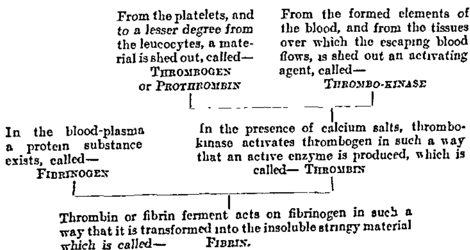
1. Slowing of the blood-stream. — This is an early phenomenon which gradually increases and may go on to actual arrest (stasis) of the blood-stream. It is dependent upon several factors, of which the dilatation of the vessels is probably one of the most important, this being brought about by the irritant *acting directly* on the *vascular wall*, or *through the intervention of* the local vaso-motor apparatus. The injurious agents which give rise to the inflammatory reactions act directly upon the endothelial cells lining the vessels. These, becoming swollen, project into the lumen of the vessels, and give rise to greater frictional resistance to the flow of the blood. Lister showed that during inflammation the red blood-corpuscles become more viscid; and Cohnheim and others have clearly demonstrated that during the process of stasis the leucocytes accumulate in great numbers in the peripheral, plasmatic blood-stream, and attach themselves to the walls of the vessels. These two factors must aid in increasing the friction. In addition to this increase of resistance in the vessels, the loss of *elasticity* and contractile power, brought about by the causal poisons and by the impairment of nutrition which act injuriously upon the various tissues in the walls of the vessels, must also aid in the production of stasis. The vessels, and especially the venules and capillaries, become unduly stretched, producing an increased intravascular pressure and a further dilatation. In consequence of the nutritive alterations in the walls of the vessels, a considerable increase takes place in the transudation of lymph, the blood-plasma becomes more inspissated, and its rate of flow may thus be decreased.

Thrombosis of minute vessels is a familiar feature of early inflammatory reactions, and is due partly *to the slowing of the blood-stream*, partly to the irregular dilatation of the lumen—this irregularity producing eddies in various sections of the vessels. An important factor in this process is the action of the poisons, which not only render the blood more coagulable, but produce destructive changes, whereby the normal smoothness of the internal lining of the vessel is lost.

As the blood-stream becomes sluggish, there is, as has already been stated, a rearrangement of the relative positions of the fluid

and the formed elements of the blood. The leucocytes and the blood-platelets fall out into the clear plasmatic peripheral stream; but, just before actual stasis, the leucocytes tend to return to the centre, and a general mixing of the elements takes place, though in all cases numbers of the blood-platelets remain at the periphery adherent to the walls of the vessels. This rearrangement of the corpuscular elements is a purely physical phenomenon. So long as the velocity of the stream is maintained at a sufficiently high standard, the formed elements occupy the axial part, but when it becomes lessened they tend to pass to the periphery. The leucocytes and blood-platelets, being of a lower specific gravity than the red corpuscles, reach the peripheral stream first, but with further slowing the red corpuscles also pass from the centre, and a mixing of all the elements takes place. The blood-platelets form the basis of all true ante-mortem thrombi, and it is because of their accumulation in the peripheral stream and their adhesion to the walls of the damaged vessels that thrombosis is so frequently seen in the early stages of the inflammatory process. The exact chemical reaction which takes place in the production of thrombi is uncertain. The blood-platelets in their staining reactions resemble the nucleo-proteins, and it is quite possible that they may be in part the source of the nucleo-protein (prothrombin or thrombogen), which, acting in conjunction with thrombo-kinase and with the fibrinogen and calcium salts normally present in the circulating blood, brings about the formation of fibrin and produces coagulation.

SCHEMA (AFTER HALLIBURTON[1]).



[1] "Handbook of Physiology," p. 451, 15th edit., 1920.

2. Transudation of lymph.—The outflow of lymph from the vessels becomes very much increased during the inflammatory process, and is one of the main causes of the swelling of the parts. This increased transudation is one of the earliest observed phenomena, and within two hours it becomes marked. The amount varies considerably, and is dependent largely upon the situation in which it occurs, though the nature and the intensity of the causal irritant, as well as the general health of the patient, play an important part in the process.

In situations where the tissues are lax (e g. about the eyelids) or where the degree of external pressure is small (e.g. in the pleural cavities) the accumulations of fluid may be very large and the swelling considerable in amount; whereas in solid tissues (e.g. the kidneys) or in situations where there is considerable external resistance (e.g. under the periosteum) the exudation may be comparatively scanty and the swelling an inconspicuous feature. From causes which are not fully understood, certain bacterial irritants cause much greater transudation than others, and the same irritant may produce at one time considerable accumulations of fluid and at other times a very scanty exudate. In a certain proportion of cases these differences are to be explained by differences in the tissues acted upon. Thus, in debilitating diseases, where there is pronounced anæmia with grave alterations in the condition of the blood and changes in the walls of the vessels, transudation occurs with great readiness. The swelling of the endothelial lining cells, the loosening of the cement substance between them, and the other degenerative changes in the cells themselves which result from the inflammatory process, produce a condition of greater porosity of the walls of the capillaries and venules. This, combined with the increased pressure in the dilated and engorged vessels, is the main cause of the increased transudation of lymph If the view that the endothelial cells lining the blood-vessels have a selective capacity in lymph transudation is accepted, it must be admitted that an alteration in this, a very probable result of inflammatory or other destructive processes, may be of considerable importance in increasing the output of lymph.

Function of the exudates.—It may be stated generally that the exudates have a decidedly beneficial action, not merely locally, but even at some distance from the site at which the irritant is acting. At and around the site, in the case of bacterial irritants at any rate, toxins and metabolic poisons are being produced, and the transuded lymph must dilute these poisons, and thus render them less harmful to the surrounding tissues and to the organism as a whole. Further, the exudates will contain the various antitoxic, antibacterial, and other protective substances which are known to be

produced by various toxic agents, and which must be present in the blood-serum. These antibodies may act locally on the bacteria, but they will, in addition, thoroughly infiltrate the neighbouring tissues, and be carried by the lymph channels to all parts of the organism. They may thus act on bacteria at distant parts, or, what is perhaps more important, antagonize the various toxic products which are being distributed throughout the body by way of the blood-stream.

The success of Bier's method of "congestive" treatment is, no doubt, due in part to this bathing and flushing of the tissues with the serum which escapes from the obstructed and dilated vessels. Wright has strongly urged this flushing of the tissues with lymph as an aid to his "opsonic" treatment; and part, at any rate, of the success of that treatment is due to the dilution of the toxic products and the carriage of antibodies, including the opsonins, to the centres of infection.

While the value of this flushing of the tissues at the region of irritation must be fully admitted, one must also recognize its danger to the organism as a whole; for, with the distribution of the protective substance, there must of necessity be also a distribution of the locally produced toxins and other poisons. In this way, therefore, these may be carried into the general circulation, and, if at all powerful, may give rise to widespread poisoning effects. Thus, it is obvious that "flushing with serum" as a method of treatment should be used with great care, and only in cases where no very active poison is likely to be disseminated.

In addition to this flushing action, the exudates loosen and separate the tissues, thus aiding the passage of the leucocytes in their protective work, and, by separating inflamed surfaces—e.g. the costal and visceral pleura—they lessen the amount of irritation and encourage the healing process. Further, the fibrin which is formed in all acute inflammatory exudates (Plate 10, Fig 1) serves to coat over inflamed surfaces, protects them, and also tends to localize the area of inflammation. Again, the fibrin acts as a sort of scaffolding during the processes of repair, holding together the two opposed surfaces, and allowing the newly formed blood-vessels and the connective-tissue cells to extend easily from one to the other.

3 **Escape of red blood-corpuscles.**—The amount of blood in inflammatory exudates varies considerably. Small accumulations of red blood-corpuscles may be seen scattered irregularly throughout the inflamed area, or the exudate may be emphatically hæmorrhagic in character. The latter condition is generally due to some constitutional condition, or to a widespread degeneration of the vessels, brought about by the action of a toxin or other

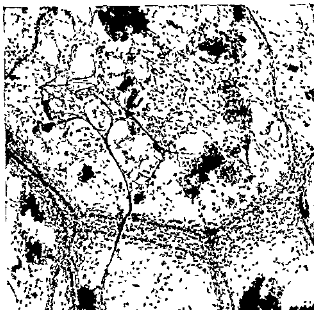


Fig 1.—Acute peritonitis—second day—showing fibrinous and cellular exudate × 60



Fig 2.—Acute abscess in the kidney, showing central cellular exudate with peripheral congested vessels and hæmorrhage. × 60.

PLATE 10.

irritant. In the more usual condition the red blood-corpuscles are found in irregular clumps close to the vessels from which they have been ejected; for there seems little doubt that these accumulations are associated with the rupture of the walls of over-distended vessels, especially those whose endothelium has undergone degenerative changes. Their common and widespread occurrence in general septic poisonings seems to point conclusively to the view that vascular degeneration is an important causal condition.

4. **The emigration of leucocytes.**—Though perhaps not the essential change in inflammation, the emigration of leucocytes is a constant feature and plays an extremely important part. As has been already stated, if a transparent vascular membrane is irritated, the leucocytes can be observed collecting in the peripheral stream of the dilated vessels and becoming adherent to their walls. If carefully watched, they are seen protruding pseudopodia through the wall of the vessel; the external part of the pseudopod gradually increases in size, and by degrees the whole leucocyte migrates to and wanders in the circumvascular tissues, eventually reaching the noxious agent or the site of damage. In most cases, migration takes place through the walls of the capillaries and venules, and is most marked at the junction of the tributaries (Plate 9, Fig. 2), the leucocytes passing between the endothelial cells, and their passage being aided by softening of the cement substance there. Though in acute inflammatory conditions the polymorphonuclear cells are the most active in the process of migration, yet it is now generally agreed that all forms of hæmal leucocytes are amœboid in their character, and in virtue of this property are able to pass through thin membranes, at any rate, such as the endothelium of capillaries. Many of them can penetrate thick layers of epithelium and other tissues, and in their passage from some of the larger veins, which certainly takes place, there must be definite migration through fibrous and muscular tissue.

THE CELLS FOUND IN INFLAMMATORY EXUDATES

The importance of cytology in diagnosis is now generally recognized, and, though I would not in any way minimize its value, I feel that very often too much is expected from it, and conclusions are drawn which are quite unjustifiable The study of the cells in various inflammatory exudates forces the conclusion that no cell is specific, and that the difference in the cells of one exudate from those of another is dependent more on the period of time the irritant has been acting than on the nature of the irritant. It is true that, in some cases, a diagnosis of tuberculosis can be confirmed by a study of the nature of the cells in the exudate, but it would be a risky procedure to make the diagnosis on the examination of the cells alone.

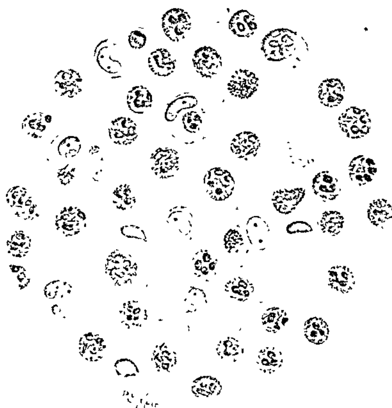
Or, again, the character of the cells in an exudate may suggest malignant disease as the causal factor, yet those who have studied the cells most fully would probably be the last to say, on such evidence, that any given case was malignant. Therefore, no excuse is needed for dealing very fully with the cytology of inflammatory exudates and, necessarily in association with it, the tissue changes which are concerned in the reparative processes.

1. **Polymorphonuclear leucocytes.**—These leucocytes, which are formed in the bone-marrow, are the principal cells of the blood, constituting about 70 per cent. of the total leucocytes. They are characterized *by a nucleus which is segmented, the lobes varying* in number, and being connected with one another by narrow strands of chromatin. The cytoplasm is fairly abundant, and shows small, irregularly scattered granules, which stain red with eosin. These *cells are formed from the large mononuclear myelocytes,* and, in the bone-marrow, various stages in the process of their evolution may be seen. In some diseased conditions—e.g. leucocythæmia—these transitional forms appear in the blood, and may pass from the blood into inflammatory exudates.

At inflammatory foci, in people whose bone-marrow is not abnormal, the polymorphonuclear leucocytes are present in about three hours after the inoculation has taken place, and become increasingly abundant in from 18 to 24 hours (*Plate 11*). This increase goes on progressively until the irritant has been overcome or the infected individual has succumbed. In cases in which these cells are able to overcome the noxious agent, there may be, compared with the other cells present, a marked diminution of the polymorphs in 36 to 48 hours (Plate 12, Fig. 1). This is still more evident in from 60 to 72 hours, and in from 84 to 150 hours the polymorphonuclear leucocytes may have completely disappeared from the exudate.

In cases where the inflammatory reaction causes death, a progressive increase of these cells takes place (Plate 12, Fig. 2). In fact, they continue to migrate in enormous numbers so long as the need for defence exists and the strain of increased production can be borne by the blood-forming tissues, the bone-marrow, etc. The imperfect and scanty production of these cells in the early stages of an inflammation often means a bad prognosis, for it points to an exhausted bone-marrow which cannot respond to the stimulus that is being applied to it, and cannot, therefore, produce the great cellular defensive agents of the body.

The time-results of the reactions which are given above are based on a series of experiments carried out by me, and are summarized as follows:—



Peritoneal exudate, 24 hours after intraperitoneal injection of B. coli communis, showing relative proportion of mononucleated to polymorphonuclear cells, active phagocytosis of bacilli, and ingestion of polymorphs and eosinophiles by the mononuclears. × 1,000

PLATE II.

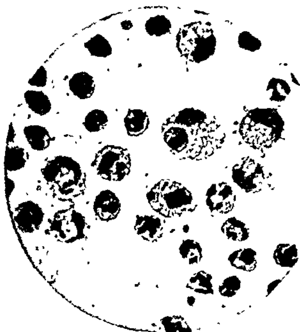


Fig 1.—Peritoneal effusion, 48 hours after intraperitoneal injection of B. coli communis, showing *pseudopodia of, vacuolation in, and phagocytosis by the* mononucleated cells × 600

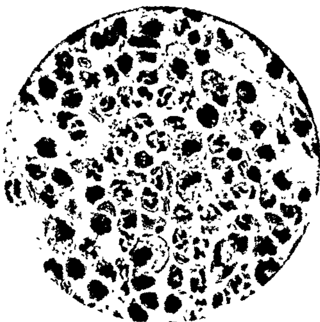


Fig 2.—Peritoneal effusion, 66 hours after intraperitoneal injection of B. coli communis *in a fatal case, showing excessive predominance* of polymorphonuclear leucocytes and comparative absence of phagocytosis × 600

PLATE 12.

SUMMARY OF TIME-RESULTS AFTER INTRAPERITONEAL INJECTION OF B. COLI

NON-FATAL CASES

10 to 20 minutes: Very few polymorphonuclear leucocytes found.
1 hour: Very slight increase in number.
2 to 2½ hours: Increase now very definite.
3 hours: A considerable number present.
4½ to 6 hours: Increase now becoming marked.
6 to 30 hours: Increase goes on during these hours, but is most marked at from 6 to 12 hours.
30 to 36 and 48 hours: The numbers now begin to diminish.
54 hours: A very pronounced diminution in numbers.
60 to 72 hours: Diminution becomes more marked.
78 hours: Very few polymorphonuclear leucocytes present.
84 to 96 hours: Still a few present.
They may persist for a few days, but from the 5th to the 7th day they entirely disappear.

FATAL CASES

The cells are found about the same time, but the increase is maintained till the death of the animal

2. **Coarsely granular eosinophiles.**—These cells are comparatively scanty in normal blood, and are easily distinguished by their brilliantly red eosin-coloured granules, which are larger and more regularly arranged than those in the polymorphonuclear leucocytes Their presence in the blood in large numbers usually indicates infection with an animal parasite, and in such cases an inflammatory exudate may contain a considerable number of these cells. In certain circumstances and in special infections they seem to take the place of, and act like, the polymorphonuclears. Thus, Opie has shown that in infections with *Bacillus pyocyaneus* there may be an abundant accumulation of eosinophiles

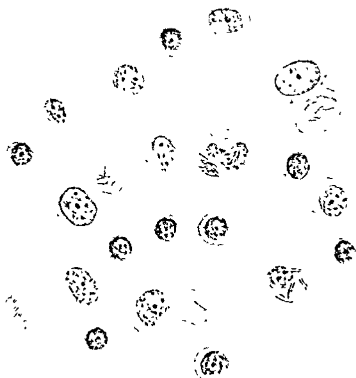
It is not necessary to enter into a discussion as to the origin of these cells, but it is important to remember that they may be found locally in abundance in cases where they are apparently not increased in the circulating blood. In mucous polypi of the nose, which are now generally regarded as inflammatory hyperplasias of the mucous membrane, eosinophile leucocytes may be found in considerable numbers. They are sometimes seen in and around inflammatory conditions of the intestine and appendix and in the submucous coat, in the base of some gastric ulcers. Again, in certain skin diseases (urticaria, pemphigus, etc.) there may be a local increase of eosinophiles, though usually in these cases the increase is also seen in the circulatory blood It has been shown experimentally that in cases of pemphigus where there was a local eosinophilia, artificially-produced abscesses showed only polymorphonuclear leucocytes. At present, therefore, the presence or absence of eosinophiles in inflammatory exudates is not of special diagnostic value.

3. **The mononucleated cells.** — This group includes a number of cells which have different origins, and possibly also different functions. Maximow has classed these under the term "polyblasts," and he states that they are derived mainly from the lymphocytes which have emigrated from the blood-vessels, though the wandering cells pre-existing in the connective tissue, and pre-existing clasmatocytes and clasmatocyte-like adventitial cells—e.g. perivascular lymphatic tissue, endothelial cells, cells of serous membranes, etc.—share in their production. This group includes the *lymphocytes*, the *mast cells*, the *plasma cells*, the so-called *hyaline leucocytes*, and other forms of mononucleated cells.

(1) **The lymphocytes.**—These have been divided into the small and the large forms, and are specially characterized by a relatively large darkly staining nucleus. The cytoplasm in the small variety is very scanty, but in the larger it is more abundant. In both it is granular, the granules being basophile and especially marked near the periphery. In acute inflammatory exudates these cells are not usually numerous, but in more chronic inflammatory conditions they, or cells which cannot be differentiated from the hæmal lymphocytes, are often very numerous and are sometimes collected in the form of irregularly shaped masses. Exudates rich in these cells, and tissues infiltrated by them, are seen especially in infection with *B. tuberculosis* (Plate 13) and in syphilis, but also are common in inflammatory conditions which have lasted for several days (Plate 14), and in which the primary state was a polymorphonuclear leucocytosis. Thus, in my opinion, an exudate rich in lymphocytes, though it may suggest tuberculosis, is not by any means diagnostic of that condition. Collections of these lymphocytes or lymphocyte-like cells are found in the tissues where the bacterial poisons or other toxins have been acting for a prolonged period (Plate 14). They are well seen in the kidney in the less acute forms of nephritis, and in the kidney and other organs in prolonged cases of infectious diseases—e.g. scarlet fever.

Whether all these cells migrate from the vessels is a matter of very great doubt, and, though migration must be admitted, I strongly hold with Adami that the collections of lymphocyte-like cells seen in the tissues and exudates are derived in the main from the proliferation of cells of a lymphoid type which are present to a greater or less extent in various situations, but especially in the perivascular tissues.

(2) **Mast cells.**—These cells are easily dist[illegible] by the presence in them of irregularly scattered basoph[illegible] which vary considerably in size. In my experience thes[illegible] t take any part in the inflamma[illegible] process, but it is [illegible] they may be degenerated fo[illegible] er cells.



Peritoneal exudate, 25 days after intraperitoneal injection of B. tuberculosis, showing bacilli in the large mononuclears, absence of polymorphonuclears, *and possible transition forms between the small and* the large mononuclears. × 1,000.

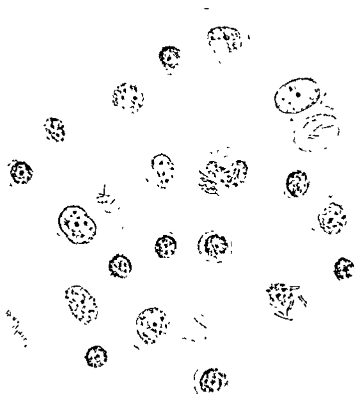
PLATE 13

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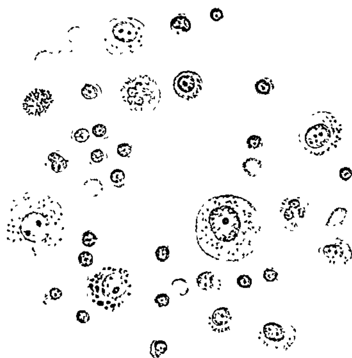
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(2) Mast cells.—These cells are easily distinguished by the presence in them of irregularly scattered basophile granules, which vary considerably in size. In my experience these cells do not take any part in the inflammatory process, but it is possible that they may be degenerated forms of other cells.



Peritoneal exudate, 25 days after intraperitoneal injection of B. tuberculosis, showing bacilli in the large mononuclears, absence of polymorphonuclears, and possible transition forms between the small and the large mononuclears. × 1,000.

PLATE 13



Pleural exudate (left side) from same case as in Plate 16, but at a later period, showing excess of small mononuclears and transitions between these and the large (endothelial) cells. There was no tubercle in this case. × 1,000.

PLATE 14.

of mononucleated cells, which are found in inflammatory exudates (Plates 13, 14).

There is no doubt that many of these cells have different origins, and possibly—though I do not think it is proved—different and specific functions. Thus, many of the mononucleated cells are derived from the tissues and not from the blood. Adami has classed these as **histogenous leucocytes**, and he includes in this group:

i. **Cells derived from serous, vascular, and lymphatic endothelium** (Plate 15, Fig. 2).—These vary much in size and in other general characters—being small, with scanty protoplasm, and a nucleus which is very rich in chromatin; or larger, with a more vesicular nucleus, and with abundant cytoplasm. The cytoplasm may be richly basophile, or it may be vacuolated, and the basophile characters may be partially obscured. Transition forms between these two varieties can be demonstrated in the tissues.

These cells are present in inflammatory exudates in the early stages, but are not numerous until about the thirty-sixth to the forty-eighth hour. In cases where recovery is likely to take place, they go on increasing until eventually the exudate may contain only this type of cell. They are actively phagocytic both to bacteria and to foreign material, such as dead cells, pigment, etc. (Plate 16). Usually less phagocytic to bacteria than the polymorphonuclear leucocytes, they are in certain cases—especially where inflammatory reaction is due to *B. tuberculosis*—the principal phagocytes of these bacteria.

Between the mononuclear cells of endothelial origin and the hyaline leucocytes of the blood we are not able to differentiate. As I have said elsewhere,[1] "all we can assert is, that transitional forms between the actively germinating endothelial cells and free mononuclears which resemble lymphocytes can be distinguished (Plate 14). There seems, however, little doubt that a considerable proportion of the mononucleated cells of inflammatory lymph are produced by proliferation of endothelial cells, though some may also be derived from cells which have migrated from the blood-vessels."

ii. **Wandering and phagocytic cells derived from other tissues.** — Besides the endothelial cells, other fixed connective-tissue cells assume phagocytic functions and show amœboid movements under the influence of inflammatory irritants. This is best illustrated in inflammation of the cornea, where the fixed corneal corpuscles swell and undergo mitosis, then become separated from their normal position and relations, and take on the characters of mononucleated amœboid phagocytes. In the exudate these cells can not be distinguished from the mononuclears which have been derived from the vascular endothelium. It seems quite reasonable to assume

[1] "General Pathology," p. 199.

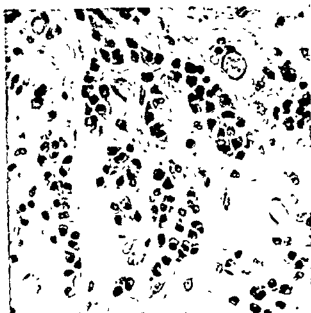
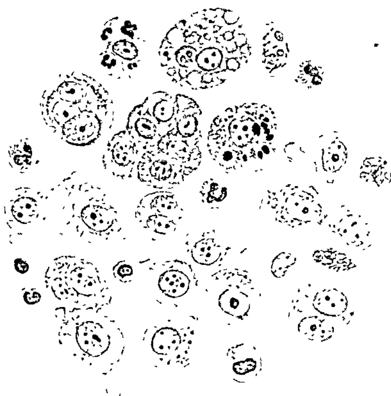


Fig. 1.—Plasma cells in the subcutaneous tissue in the neighbourhood of a wound × 400



Fig. 2.—Omentum, 21 hours after intraperitoneal injection of Bacillus Flexner, showing a vein filled with cells mostly of the mononuclear type. *a*, Swollen and endothelial cells × 600

PLATE 15.



Pleural exudate (acute pleurisy, right side) from same case as in Plate 14, showing phagocytosis by mononuclear cells which are shed endothelial cells, or at any rate cells indistinguishable from these. × 1,000.

PLATE 16

that other fixed connective-tissue cells may act in the same way as these corneal corpuscles.

iii. **Clasmatocytes.**—The origin of these cells, which were first described by Ranvier, is uncertain. They are large, irregular cells, which are elongated and show numerous branching processes (Plate 17, Fig. 1), being probably concerned in the amœboid movements of the cell. The nucleus is oval and the cytoplasm contains irregular basophile granules, which Ranvier regarded as stored-up secretion He maintained that they came from the blood, and were modified leucocytes. According to Marchand, they are "primitive wandering cells" in the tissues.

They resemble the modified corneal corpuscles described by Senftleben and by Councilman in their work on inflammation of the cornea; and, in what may be regarded as their resting stage, they appear as mononucleated cells, resembling those derived from endothelial and connective-tissue structures.

iv. **Fibroblasts.**—These spindle-shaped cells are derived from the mononucleated cells, though there is much difference of opinion as to which kinds of mononuclears are concerned in their formation. They are developed only in the later stages of acute inflammation and in the more chronic conditions, and are rather cells concerned in the process of repair.

v. **Giant cells.**—Cells with several nuclei are common in all inflammatory conditions (Plate 17, Fig. 2), and are most numerous in the late stages. Many of these are formed by fusion into plasmodial masses of endothelial or other forms of mesoblastic cells, though some seem to result from an aberrant cell-growth where the nuclei undergo division without the protoplasm following suit. They are amœboid and actively phagocytic, are specially well developed where resistant tissues (e.g. bone) have to be absorbed, and they form a special feature of certain chronic inflammatory conditions (e g tuberculosis, syphilis, etc).

Phagocytosis and the function of the leucocytes.—The term "phagocyte," which was introduced by Metchnikoff, is applied to cells that ingest foreign materials, bacteria, and other cells, and, by a process of intracellular digestion, bring about the solution of certain of these ingested particles It has been shown that the process of phagocytosis is almost a universal endowment of cell-life, and by many authorities it is considered to be the most important defensive agent against disease or disease-producing products, and likewise an essential factor for the carrying on of cell-life. In physiological conditions phagocytosis is a constant feature, for the moulding of the tissues (e.g the bones) is largely brought about by the action of these phagocytic cells, and waste products of various kinds are removed by them. There seems also little doubt

As has been stated, this emigration is towards some attractive force which is possessed by most bacteria. Experimentally, it has been shown by Leber and others that certain products of bacterial activity and tissue metabolism, as well as certain chemical and physical agents, attract wandering cells, whilst others have no such attractive power. Glass tubes closed at the outer end and containing chemicals were carefully introduced into the blood-vessels, and the movement of the cells into these tubes was observed It has been shown that various compounds of mercury, as well as turpentine, finely powdered copper, and other substances, exert a *positive* attraction, whilst quinine, chloroform, glycerine, alcohol, etc., act negatively; that weak solutions sometimes act positively, while strong ones have a negative action. The toxins of most of the pathogenetic bacteria, if not too concentrated, attract leucocytes in great numbers; whilst, if they are concentrated, leucocyte emigration is greatly hindered. This positive and negative chemiotaxis, as it has been called, can be well illustrated by a very simple experiment.

The exposed mesentery of a frog is washed with normal saline solution: the leucocytes show increased amœboid activity, collect at the periphery of the vessels, and migrate through the walls to the surface of the mesentery. If, however, the exposed mesentery be at once washed with a weak solution of quinine instead of normal saline, the leucocytes, as Binz has pointed out, remain globular, and do not become adherent to the walls. To prove that it is not merely a paralysis of the leucocytes which occurs, as Binz at first thought, it is only necessary to remove the leucocytes from the vessels to see their amœboid movement again becoming quite evident. Thus the quinine has converted a previous *positive* into a *negative* chemiotaxis.

Associated with the microphages in their phagocytic work are the macrophages. These large mononucleated cells appear moderately early in any inflammatory exudate; but it is not till about forty-eight hours or more after the injury that they become very active. They appear to be the "scavengers" of the tissues, and are concerned largely with the removal of dead, degenerating, or degenerated products. The ingested material is often seen in the cytoplasm of the cells to be surrounded by a clear space (Plates 11, 13, 18), which contains fluid having an acid reaction. In these "vacuoles," which may be numerous, the included bacteria, the polymorphonuclear or other cells, the fragments of degenerating and dead tissue, etc., undergo gradual solution and absorption (Plates 11, 13, 14, 16, 18). The nuclei of the ingested cells become fragmented, and later the chromatin particles undergo complete solution or digestion (Plate 18). This is followed by a gradual disappearance of the cytoplasm. The red blood-corpuscles shrink, and their hæmoglobin may either be

absorbed, or may remain as pigment within the phagocyte. The bacteria lose their staining reactions and are gradually dissolved.

In some cases, and especially with certain bacteria—e.g. *B. tuberculosis* and *M. gonorrhœæ*—the organisms may remain in the cells for a long time with few or no destructive changes taking place in them, and in some cases it would appear as if they were capable of *actively proliferating*.

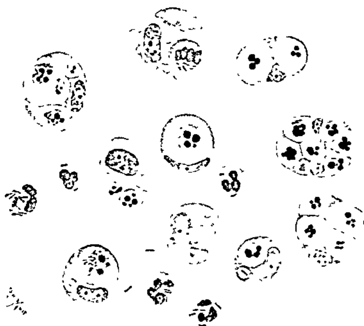
The relationship between phagocytosis and virulence of the organisms is somewhat indefinite; but it may be stated as a general rule that the more virulent the organism the less is the amount of phagocytosis, and the later is it in making its appearance.

Extracellular action of the cells of inflammatory exudates.—That living bacteria can be ingested by these phagocytes there is, I think, no room for doubt; but it seems to be equally clear that various substances contained in the blood and in the lymph have an injurious action on living organisms, inhibiting their action in some way, and thus rendering them a more easy prey to the leucocytes.

Metchnikoff and his followers consider that the emigration of leucocytes and their intracellular action are the essential changes in inflammation, and that the vascular and other phenomena are mere auxiliaries. They maintain that the pathogenetic bacteria are destroyed in the phagocytes by a process of intracellular digestion. Nuttall was the first to show that the blood-serum had a markedly bactericidal effect, and this observation has been abundantly confirmed by other workers. It is not necessary to deal here in detail with the great and important facts which have been elicited by further studies on this subject. Suffice it to say that the evidence is quite clear that the body fluids may contain various substances which have an injurious effect on certain bacteria and a neutralizing effect on their products. These opsonins, agglutinins, antitoxins, and other antibodies are of the greatest importance both in the diagnosis and treatment of disease. The various substances are derived from the cells—some, no doubt, from the polymorphonuclear leucocytes; but the other hæmal leucocytes, as well as the fixed cells of the body, are probably concerned in their production.

INFLAMMATION IN NON-VASCULAR AREAS

The phenomena of inflammation in non-vascular areas are best studied in the cornea, and in this description I follow the work of Senftleben and of Councilman. The cornea is a transparent, non-vascular membrane, the fibrous tissue of which it is mainly composed being arranged in parallel layers, between which are numerous lymph spaces and channels. The branched connective-tissue cells—the *corneal*



Peritoneal exudate, 48 hours after intraperitoneal injection of B. coli communis, showing stages in the degeneration of the ingested polymorphonuclear cells. × 1,000.

PLATE 18.

corpuscles—are found flattened between these layers. The lymph channels communicate freely with one another and with the peripheral lymphatics of the cornea.

If the injury is very slight, none of the ordinary phenomena of inflammation may be induced, and repair may be effected merely by a proliferation of the corneal corpuscles. If the process is carefully watched, the corneal corpuscles at the centre of the injured area are seen to undergo degenerative and destructive changes, while those near the periphery become swollen and may show proliferative changes. The proliferation, however, is mainly seen in the peripheral healthy corpuscles. These send offshoots into the necrosed zone, and gradually bring about complete repair of the damaged area. With more extensive damage all the ordinary inflaatommry phenomena may be developed, some with greater intensity than others. An area of opacity is formed with the damaged focus for its centre, this opacity being largely due to the accumulation of polymorphonuclear leucocytes and to the swelling of the corneal tissue brought about by the imbibition of fluid which has transuded from the vessels The vessels at the periphery of the cornea become dilated and engorged with blood, and from these vessels, as well as from the dilated conjunctival vessels, leucocytes pass out in considerable numbers and migrate, on the surface of the conjunctiva and between the fibrous laminæ, to the damaged area. The corneal corpuscles show well-marked proliferative changes, and in the cellular exudate which is produced these corpuscles may appear as mononucleated phagocytes, which are indistinguishable from other mononucleated cells derived from the blood-stream or from the fixed tissue cells—e g. endothelium—of the part. If the inflammation lasts for four or five days, numerous small round cells, resembling lymphocytes, are seen in the exudate. According to Adami, these are cells which have migrated from the sheaths of lymphoid tissue that surround the vessels. If the inflammation continues for long periods, new vessels are formed by budding from the pre-existing peripheral vessels, and these pass into the non-vascular cornea, right up to the edge of the inflamed area, which usually at this stage has become an ulcer. Healing takes place, and a white opaque fibrous cicatrix may always mark the site of the inflammation. Very commonly, too, the newly formed vessels in the cornea do not completely disappear during the healing processes, and may be observed in man for years afterwards.

INFLAMMATION IN LYMPHOID TISSUE

The swelling and acute tenderness of glands as a result of septic absorption from a wound is one of the most familiar conditions with which the surgeon has to deal. Lymphatic tissue appears to be

especially susceptible to the reactions which are called inflammation, this being due, no doubt, to the arrest by the glands of the bacteria or their products which are being drained from the wound by the lymphatics. Lymphatic tissue is very widely distributed throughout the body, and as a result of inflammation many definite lymphoid nodules become evident which were previously microscopic in size. These lymphatic areas, whether they are in the form of glands or not, not only act as local defenders of the body, but they also supply cells which migrate to distant parts for the purpose of attacking the invading organisms in the foci at which they have settled down.

During the inflammatory and proliferative processes the glands become swollen, reddish in colour, and softer in consistence. More minute examination reveals the dilatation of vessels (hyperæmia), the transudation of serum, and the emigration of leucocytes. The extent of the leucocyte invasion is not easy to determine, unless migration of the polymorphonuclear leucocytes is well marked. Proliferation of the cells, not only of the lymphoid tissue proper, but also of its supporting connective tissue, takes place, and, as has been already said, many of these cells may pass from the glands and migrate to any seat of injury.

INFLAMMATION IN BONE

The changes which occur in inflammation in bone are identical with those which occur in any of the other tissues of the body; but the resistant character of the tissue prevents any marked exudation from occurring, so that swelling is not a pronounced feature. Pain is usually severe, this no doubt being due in part to the pressure, by the inflammatory exudate, of the nerve-endings against the resistant tissues. Pain may result from the action of the toxins on the nerve-endings; and in inflammation of bone, the transudation of fluid being limited, the toxin acts with greater intensity because the flushing and diluting action of the exudate is at a minimum.

TYPES OF INFLAMMATION AND CHARACTERS OF INFLAMMATORY EXUDATES

Various forms of "inflammation" have been described, and it is necessary therefore to discuss them. The exudates vary in quality and quantity according to the tissues into which they are poured, and the nature and intensity of the inflammatory agent. Thus, the exudates into serous cavities or into loose subcutaneous tissues may be very considerable in amount; while those into dense tissues may cause hardly appreciable swelling of the part. Further, the exudates may be serous, fibrinous, hæmorrhagic, or purulent, these characters being dependent on the nature of the irritant and its intensity of

action. In all cases the exuded fluid is richer in protein than the ordinary lymph, and may contain digestive ferments, bactericidal substances, etc.

1. **Acute serous inflammation.**—This condition is one in which the transudation of lymph from the vessels is the salient feature, the emigration of leucocytes being only slight in degree. Thus fibrin-formation does not take place or is present only to a slight extent. All the essential phenomena which have been described above are present, though not in the same degree or intensity.

The serous exudate occurs especially in the milder forms of inflammation, but in some virulent infections the exuded fluid may be serous in character. The fluid contains few cells, practically no fibrin, but is richer in albuminous substances than the lymph. These exudates, as I have already stated, bring about a dilution of the toxins, and at the same time separate the elements of the tissue from one another They may be carriers of protective substances to adjacent or even to distant parts by way of the lymphatics. Though these exudates are in the main favourable, yet in certain cases the swelling caused by them may give rise to grave symptoms—e g swellings about the glottis, causing suffocation.

2. **Inflammation affecting serous surfaces; acute fibrinous or sero-fibrinous inflammation.**—In this form of inflammation one of the earliest changes is a swelling and a loosening of the covering endothelial cells. These become discharged and are found along with the various forms of leucocytes in the exudate. The vascularization of the part is especially exhibited in the subserous connective-tissue layer, and it is from the dilated vessels of this region that the emigrated leucocytes which are very abundant, mainly come The pronounced formation of fibrin which occurs in this condition is in part due to the denuding of the surface endothelium, though the breaking down of the large number of leucocytes which have passed out of the vessels is the main factor. The transudation of serum may be very slight, or it may be more abundant. It would appear that in these cases the irritant either has a special action on the endothelium of the vessels, causing its destruction, so that the leucocytes can pass out more easily, or has a special positive chemiotactic influence on the leucocytes. The exudate is rich in leucocytes, fibrin is present, sometimes in considerable abundance (Plate 10, Fig. 1), but the serum is small in quantity, and in consequence the surfaces on which the deposit occurs become covered with a granular or velvety layer of greater or lesser thickness, which in its early stage can be readily stripped off. In this layer many of the cells are necrotic leucocytes, but endothelial and other cells may also be present.

In serous cavities, fibrinous exudates often appear to restrict the spread of the disease, and the fibrinous adhesions which are formed may confine the infection to its seat of origin Thus, in the peritoneum the adhesions between the coils of the intestine frequently have a very definite localizing action on the spread of the inflammatory process. These sero-fibrinous or fibrinous exudates may occur in almost any situation, but are especially seen in serous cavities and on mucous surfaces.

3. **Suppurative inflammation.**—Though suppurative inflammation will be described by another writer (p. 188), it is convenient to deal with some of the main points here, so as to establish the definite association between this form and those already described.

As in the fibrinous form, the leucocyte emigration is the essential feature; but owing, in many cases, to the continued action of the bacteria, or to the want of protective reaction on the part of the tissues, the bacteria for a considerable time hold sway and the cells undergo degeneration and death. Thus there is produced at the focus a thick, more or less creamy and opaque fluid (**pus**), which is composed in the main of polymorphonuclear leucocytes, some of which show quite regular nuclear staining reactions, and have in their cytoplasm foreign material, especially bacteria, in all stages of degeneration. Others show badly-staining, broken-up nuclei. Mononucleated cells derived from the blood and from the fixed tissue elements may also be present in greater or lesser numbers. In addition, there is always partially digested necrotic tissue. Fibrin is usually absent, and the causal bacteria may or may not be present, they, in the later stages, have become completely disintegrated Thus "sterile" pus is not uncommonly found The absence of fibrin is generally attributed to the disintegration of the proteins, of the necrotic tissue, and of the cells by ferments developed by the pathogenetic bacteria or derived from the cells. These proteolytic ferments cause a liquefaction of the various elements, and this liquefied and partially degenerated material constitutes pus. The pus, in addition to the ferments, peptones, and bactericidal substances, may contain cholesterin crystals and fatty acids, as well as pigment derived from red blood-corpuscles or produced by chromogenetic bacteria. There seems little doubt that in the vast majority of suppurative inflammatory reactions in the human subject bacteria are, or were, present; but it must be admitted that pus may be produced experimentally by the injection of certain chemical irritants, such as turpentine, or the salts of mercury and copper, as well as by the products of the growth of certain bacteria. The suppurative conditions which sometimes follow the intramuscular injection of mercury in cases of syphilis, or the subcutaneous injection of antitoxin, may be aseptic; but the ease with which organisms can gain admission from the superficial parts of the skin renders it

difficult in many cases to estimate the relative parts played by the bacteria and the chemical irritant.

After the introduction of bacteria to the tissues, there is a period during which no reaction is observed, but in which the bacteria are multiplying and producing their toxins. When this process has reached a certain stage the definite reactions of inflammation are exhibited. The capillaries of the part become dilated and engorged with blood. There is transudation of lymph, and emigration of leucocytes, this latter phenomenon being so extensive that at the inflammatory focus the immigrated cells completely obscure the tissue cells. They show marked phagocytosis to the bacteria, and at the same time, probably owing to the action of the toxins produced by the bacteria, many of them undergo degenerative changes and ultimately become dissolved (Plate 187) As long as the reactive processes in the tissues of the body are not able to overcome the bacteria, the emigration and subsequent destruction of the leucocytes will continue. Thus the suppurative inflammation may go on spreading indefinitely. When, however, the bacteria have been conquered by the tissue cells, a localization of the destructive area is seen and an *abscess* produced, the outer wall of this being a mass of leucocytes in which the degenerative changes are not marked, while the central part consists of degenerated and partially dissolved leucocytes and tissue fragments. Living bacteria may still be present, but their activity and their number are much diminished.

In suppurative inflammation of serous surfaces, the fibrinous deposit which forms in the early stage of the inflammatory process may localize the bacteria, and thus the pus-formation may be confined to a small area. Such localized suppurative conditions are found in the region of the appendix. At later stages the fibrin may become dissolved and a general spreading inflammation be produced, but in a considerable proportion of cases the fibrinous adhesions may remain intact until the active period of the bacteria has come to an end and the acute inflammatory process has subsided.

4. **Hæmorrhagic inflammation.**—Blood, in varying quantities, may be found in all classes of inflammatory exudates, though in some it may be so abundant and occur so early that the exudate may be regarded as a definitely hæmorrhagic as distinguished from a serous, fibrinous, or purulent one Such exudates usually indicate extensive changes, particularly of a fatty nature, in the endothelium of the capillary walls, due to the intensity of the primary lesion or to previous degenerative changes in the vascular system, or in the blood and the blood-forming organs. They occur especially in positions in which the capillaries are not well supported—e.g. in the lungs and on serous surfaces.

5. Inflammation affecting mucous surfaces.—The types of inflammation affecting mucous surfaces, or affecting surfaces lined with secreting epithelial cells, are most conveniently dealt with under the subheadings of Membranous and Catarrhal Inflammations (*see* below). There are, however, common characteristics of these two types, as they affect mucous surfaces, to which reference must be made.

The hyperæmia, the transudation of serum, the emigration of leucocytes, all occur in the submucous tissues, but they are more or less confined to those tissues by the definite basement membrane. The mucous cells are stimulated to produce increased amounts of mucin, and thus the discharge is mucinous rather than fibrinous. Many of the mucous cells, partly as a result of the toxins, and partly as a result of over-stimulation, undergo degenerative changes. If the inflammation is only moderate in intensity, the mucin will be abundant, the cast-off cells and the leucocytes relatively scanty (*catarrhal inflammation*); but if, on the other hand, the reaction is intense, there is necrosis and death of the mucous cells and the production of a distinct membrane composed of these cells, of leucocytes, and of fibrin (*membranous inflammation*).

(*a*) Membranous inflammation.—This term is applied to cases in which, as a result of the inflammatory changes, there is formed a *definite membranous structure* This membrane, or, more correctly, *false membrane*, is composed of inflammatory exudate and necrotic tissue, and occurs especially on mucous surfaces—e.g. the throat, the intestines, the bladder—but it may also be found on superficial wounds. The causal irritant is either in or on the superficial layers of the affected tissue. The vessels show marked engorgement, the transudation of lymph and leucocytes is considerable, and the exudate forms a coagulum with the superficial cell-layers which have become necrotic. The membrane is at first more or less adherent to the deeper tissues, but by constant accumulations of leucocytes in the deeper parts it becomes gradually separated.

Adami states that "where there exists a well-formed basement membrane the diffusion inwards of toxins is arrested to a considerable degree, only the surface epithelial layer undergoing necrosis and being cast off."

The term *diphtheritic* is often applied to this form of inflammation, but, as many of the cases are not in any way related to the organism of diphtheria, the term membranous is, in my judgment, much to be preferred.

(*b*) Catarrhal inflammation.—The essential changes in this form of inflammation are proliferation, desquamation, and degeneration of the epithelial secreting cells, the proliferative changes being in

excess of the degenerative ones. The change is found in its most intense degree in mucous membranes. The vessels in the deeper parts always show engorgement, and there are, in addition, transudation of lymph and emigration of leucocytes, both of these phenomena being often present to a considerable degree. The secretion of the cells is always increased in amount, and is watery or mucous in character. Examination of the exudate shows that it contains numerous leucocytes, and also epithelial cells which may show proliferative changes as well as degenerative ones. All forms of cells may exhibit phagocytosis to other cells or to foreign particles—e.g. blood pigment, etc.

6. **Interstitial inflammation.**—In this condition, as the term is generally [illegible] of connective tiss[illegible] of the part. Th[illegible] irritants acting slowly, but it may be brought about by special strain, or it may be a sequel of chronic degenerative and absorptive processes. In this process the fibrous tissue is at first cellular, and collections of small lymphocyte-like cells may be seen at various points; but the usual phenomena of inflammation—dilatation of vessels, lymph transudation, leucocyte emigration, etc.—are absent.

The condition is rather that of a hyperplasia than of a true inflammatory reaction, and is well illustrated in the overgrowth of fibrous tissue which takes place in the lungs, in the liver, or in the kidneys as a result of the irritation caused by foreign particles or by bacterial or metabolic poisons. Thus, anthracosis in the lungs and cirrhosis in the liver are typical examples of "interstitial inflammation."

7. **Parenchymatous inflammation.**—The changes are of a degenerative and not of an inflammatory character, though they are very commonly associated with inflammation, and may be brought about by the direct action of toxins on the tissues. They may, however, also result from impaired vascular supply, or from altered metabolic processes. Though mainly a change in the functioning cells of a part, the condition is practically always associated with changes in the supporting tissues and in the vessels. The cells become swollen and the cytoplasmic reticulum becomes more evident, producing the so-called "granular" appearance. The nucleus may show evidences of degenerative changes in varying degrees. The vessels are usually dilated, and the supporting tissues may be swollen and may show infiltration with leucocytes.

THE CAUSES OF INFLAMMATION

Bacterial.—In the vast proportion of cases of acute inflammation, bacteria are the direct exciting cause. The micro-organisms gain

admission in various ways, and by their irritant action, or the irritant action of their toxins, induce leucocyte emigration and the other inflammatory phenomena which have been described. Even in cases where the exciting irritant has been thermal, chemical, or mechanical, and where the destructive and reactive conditions are the result of wounds, burns, corrosive agents, or foreign bodies, the secondary results are often those which call especially for surgical intervention, and they are most frequently caused by the introduction of bacteria to the damaged area. Thus, in emphysematous gangrene it is well established that the causal organism is especially virulent in wounds in which there has been considerable destruction and laceration of the muscular tissue. The pathogenetic bacteria are the causal factors in the majority of cases in the human subject, but it must always be remembered that saprophytic bacteria may lodge in any wound and, though not causing any definite inflammatory reaction, may hinder the healing process. These bacteria, then, are important from the point of view of the surgeon, and it may be said that surgical antisepsis is largely directed to the destruction of these organisms both in the wounds and in the surroundings of the operative area. These saprophytic or putrefactive bacteria may give rise to gas-production in the tissues, and the "foul pus" of empyemas and similar suppurative conditions is generally produced by them.

Further, in inflammatory conditions we have to consider the bacteria which are normally present in the skin and on mucous surfaces, and which may in special circumstances assume pathogenetic functions—e g. some of the intense inflammatory conditions of the alimentary canal are undoubtedly due to *Bacillus coli*.

In regard to the production of inflammation by bacteria in any given case, two main factors have to be considered—the resisting power of the individual tissues and the virulence of the organisms. It has been firmly established that the tissues can destroy, by virtue of the bactericidal power of their fluids as well as by the phagocytic power of their cells, considerable numbers of bacteria, and that this destruction is more marked if the bacteria have a feeble resisting power. Any condition, therefore, which lowers the resisting powers of the tissues, or lessens the bactericidal activity of the body fluids, must render the individual more susceptible to attack by bacteria, and will probably intensify any inflammatory reaction which is set up. Again, it is a well-established fact, which we need not discuss here, that more intense reactions may be produced by one type of bacteria than by another; and that one form of organism may produce even in the same individual two or more different conditions —e.g. streptococci may produce spreading inflammatory conditions or localized abscess-formation or necrosis.

Traumatic.—Under this term may be included mechanical, thermal, and chemical causes, as all of these act as direct irritants upon the tissues and bring about cell-disintegration. The products of this cellular degeneration may in their turn act as additional irritants, and so the inflammatory reactions may be definitely set up or accentuated. Among the mechanical causes must be included all wounds, bruises, and fractures, the intensity of the resulting inflammation depending to a considerable extent upon the nature of the injury. Thus, in clean surgical wounds all the phenomena of inflammation are seen, but they are present only in a minor degree, whereas very extensive and very severe reactions may follow lacerated wounds or bruises or fractures. This same variation in reaction is illustrated in burns and in frost-bites, the resulting tissue-changes being only slight or very severe.

Of the chemical irritants, even weak solutions of corrosive sublimate or carbolic acid may give rise to severe reactions, and may bring about the death of considerable areas of tissue. Among these chemical irritants, certain toxins produced by plants and animals must be included. The stings of insects, the venom of snakes, and such substances as mustard, cantharides, croton oil, etc, are capable of producing all the reactions of inflammation.

Nervous.—Though we regard with scepticism the frequently expressed opinion that nerve action, *per se*, can set up inflammatory reactions, yet it must be admitted that many conditions which can at present be attributed to nervous causes alone cannot be distinguished from inflammation. Thus the pathological anatomy of the condition of *herpes zoster* allies it with inflammation, and yet all the evidence seems to point to the cause being a disturbance of the posterior root-ganglia Again, various types of *erythema* are regarded as nervous, and they certainly show many of the inflammatory phenomena, though some of these—e g leucocyte emigration—may be only slight.

Most surgeons are familiar not merely with "referred pain," but with what may be called "referred inflammation"—i.e. areas of redness or actual inflammation occurring at some distance from a primary focus, but both being in the distribution area of a particular nerve. It is possible in these cases that the nerve itself has no special action, but that the infection is caused by means of lymphatics in the nerve-sheath. Adami maintains that in many of these cases the poisons themselves are not the direct cause of the inflammatory manifestations He holds that "the irritation of a sensory nerve of the primarily inflamed area influences the whole of the neuron of which it is a part." Thus, the irritant action is distributed by the branches of the nerve, and so the vascular and other changes which are the important feature of the primary focus must be regarded as the result of reflex action.

CHRONIC INFLAMMATION

The term "chronic inflammation" is used to denote at least two different conditions. In one it is applied to the results produced by an inflammation which has lasted for a long time, but in which the acute reactions, though present, are not marked; in the other, to conditions in which the main change is an overgrowth of fibrous tissue resulting from a slowly acting irritant or as a sequel of degenerative changes.

In the first type of case all the ordinary phenomena of inflammation are present to a greater or less extent; the inflammatory exudate is produced, and this undergoes organization, and may eventually be converted into dense fibrous tissue, by the processes which will be dealt with in the section on Repair (p 169). Side by side, however, with these reparative processes the degenerative and inflammatory ones go on.

It is common to speak of chronic peritonitis or chronic pleurisy when we merely mean the results of an acute process, the whole of the inflammatory, degenerative, and reparative processes having subsided. This should be clearly differentiated from true chronic inflammation, where all the processes are going on side by side, though the reparative are usually in excess of the destructive ones. There are numerous examples of this form of chronic inflammation, but perhaps the best examples are found in diseases of bone, where the reparative overgrowth is seen in the marked thickenings which are constantly present.

A similar chronic inflammatory condition may be due to special organisms that have a low grade of virulence, or, at any rate, produce a weak toxin which acts slowly on the tissues. Such chronic inflammatory conditions are characteristic of tuberculosis, syphilis, leprosy, glanders, actinomycosis, etc. In these conditions the ordinary inflammatory phenomena are present, but the special feature is a production of granulation tissue resulting from a proliferation of the vessels and the cells of the part. In this form of chronic inflammation there may be exhibited certain special features, such as necrosis and giant-cell formation, these giant cells being formed by a fusion of mononucleated cells.

In the second class of cases the special characteristic is the production of new tissue for the purposes of regeneration or replacement of old tissue. The condition is rather one of hyperplasia than of inflammation. The ordinary reactions which are seen in acute inflammation are absent.

As a general rule, the connective tissue which has replaced the old tissue is seen in the early stages of its existence as granulation tissue. Subsequently it undergoes various changes, which need not be described

here, being eventually converted into fibrillated connective tissue. This hyperplasia is frequently seen in mucous membranes which are the seat of some chronic irritation, the various elements of the mucosa, but especially the lymph-nodes, becoming thickened and often fibrous Chronic interstitial overgrowth of fibrous tissue is seen in the lungs in cases of anthracosis, silicosis, syphilis, glanders, etc., without any accompanying acute inflammatory changes, and a similar overgrowth of fibrous tissue occurs in the liver, kidney, etc., in the so-called chronic interstitial inflammations (cirrhosis of the liver, chronic interstitial nephritis, etc.). The essential changes in all these cases are degeneration and necrosis of the specially functioning elements, and a replacement of these by tissue which is at first cellular, but later definitely fibrous. It is true that leucocyte emigration and other inflammatory phenomena often occur around these areas of what Adami calls "replacement fibrosis," but we regard these as secondary to the degeneration and necrosis.

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THE CLINICAL COURSE AND TREATMENT OF INFLAMMATION

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The causation and the pathology of inflammation having been discussed in detail in the preceding article, it is intended now to view the phenomena of inflammation from the clinical standpoint; to show by what local and constitutional signs and symptoms the surgeon is enabled to infer the presence of the various pathological processes which constitute inflammation; to point out how these processes may terminate; and, finally, to discuss the means which the surgeon has at his disposal to restore the inflamed parts to their normal condition. As pathologically, so also clinically, acute and chronic inflammation are so far removed in their manifestations that they need separate consideration.

ACUTE INFLAMMATION

Local symptoms.—The local signs of acute inflammation can be grouped under five headings:

1. Redness.
2. Swelling.
3. Heat.
4. Pain.
5. Interference with function.

The first four of these have from time immemorial been looked upon as the cardinal signs of inflammation; they are the "*rubor et tumor cum calore et dolore*" of Celsus.

1. Redness.—This is due to the increased amount of blood present in the vessels of the inflamed area. In the earlier stages there is a bright-red blush of the skin, disappearing with the pressure of the finger and rapidly returning as the pressure is removed. After a little time it is found that while the colour disappears, on removal of the pressure it returns but slowly: the vessels of the part are dilated, but the blood-flow through them is slow. At the same time the decreased rate of blood-flow leads to less perfect oxygenation of the blood in the region of inflammation, and the colour changes from a bright to a dusky red. Later, the colour becomes still darker and assumes a purplish tint; pressure with the finger no longer empties

the vessel, and the colour is not caused to disappear: stasis, or even thrombosis, has occurred. In some of the more acute forms of inflammation mottled red patches are present, where the red corpuscles have made their way in large numbers through the damaged walls of the vessels. In non-vascular tissues the redness must be looked for in the neighbouring vascular parts; the hyperæmia and congestion of the conjunctiva in corneal ulceration is one of the best-known examples of this phenomenon. After the subsidence of an acute inflammation the restoration of the vessels of the affected area to their normal condition may occupy weeks or months, and consequently the redness is of like duration; moreover, when large numbers of red corpuscles have escaped into the tissues around the vessels, permanent pigmentation may remain.

2. **Swelling** is dependent in the first place upon the increased amount of blood in the part; but very soon exudation of fluid and cells from the distended blood-vessels takes place, and the swelling becomes more obvious. When the skin pits on pressure in a case of acute inflammation, exudation into the tissues immediately beneath it may be inferred. The amount of exudation which takes place is dependent chiefly upon the laxity or density of the tissues involved. Thus, in abscess of the palm the dense subcutaneous tissue, intersected everywhere by tough fibrous bands, is capable of receiving only the smallest amount of exudation, and the swelling is comparatively slight. Similarly, inflamed bones cannot themselves swell in response to inflammation, and any enlargement detected by examination is due to exudation into or beneath their periosteal covering. On the other hand, exudation into the lax tissues of the eyelid or the scrotum may give rise to the most exaggerated degrees of swelling. Neglect to bear in mind this differing tendency to exudation may lead to error. Thus, to recur to the first-quoted example, of a palmar abscess, while it is true that the palmar swelling is slight, there may be a very advanced degree of tumefaction of the tissues on the dorsum of the hand, which may distract attention from the real site of the affection. As a further example may be mentioned the swelling of the eyelid which may accompany an inflammatory focus on the scalp hidden from view by the hair. It will be understood from what has been said that the amount of swelling is therefore not necessarily an index to the severity of the inflammation.

3. **Heat** in inflammation is both a subjective and an objective phenomenon. To the patient it is evident by the characteristic burning feeling, whilst the surgeon may readily appreciate its presence by placing his hand over the inflamed part. The use of a thermometer will show readily a difference between the temperature of the skin over the area of inflammation and the normal skin at a distance. As is stated later, inflammation is associated with a rise

of temperature of the body generally, but the condition now under consideration is the difference in temperature between the inflamed area and the other parts. This local heat is due to hyperæmia, and not to any local production of heat; hence the local temperature never rises above that in the left ventricle. Elaborate experiments have been made with a view to deciding whether there is any actual production of heat locally as the result of inflammation, and it may be taken as proved that any such production is of the slightest, and is incapable of affecting the general body-temperature.

4. **Pain** is a prominent and almost constant feature of acute inflammation. It is due to pressure on the sensory-nerve terminals, as a result of hyperæmia and exudation, and it is probable that the inflammatory process renders these hypersensitive. The degree of pain is dependent not so much upon the amount of hyperæmia and exudation as upon the tension—that is to say, upon the ability of the inflamed part to expand in order to accommodate the distended blood-vessels and the surrounding exudation Thus, inflammatory exudation into dense tissues such as the palm of the hand, or into a bone, or beneath firm and unyielding structures such as the popliteal fascia, will cause the greatest pain; exudation into an eyelid or beneath the lax skin of the forearm is, however, comparatively painless. It may be said, therefore, that the pain of exudation varies inversely with the swelling. The *character* of the pain differs with the tissues affected; thus, it is burning when the conjunctiva is affected, stabbing in the case of the pleura or the peritoneum, and aching in inflammation of bone.

5. **Interference with function** is invariably present. This is due partly to the pain caused by use. The inflamed eye cannot bear the light, and the patient cannot move an inflamed hand. Exudation, deranged blood supply, and damage to the constituent cells of the part also have their share in this impairment of function, as shown in the cessation of function of secreting glands, or the imperfect contraction of an inflamed muscle.

Constitutional signs.—Accompanying the local inflammatory process, certain general or constitutional signs are present in greater or lesser degree. These signs, grouped together, may be designated by the term "fever." Before proceeding to describe them in detail, it is necessary to consider the agency by which a local inflammation gives rise to systemic disturbance. The majority of inflammatory processes are due to the presence of micro-organisms, and in these cases it is the absorption into the circulation of the toxins produced by the growth of these organisms which is responsible. That such is the case has been proved by the production of fever by injecting into the circulation the products of growth of artificial bacterial

cultures. It is, however, undoubted that febrile symptoms may follow aseptic inflammatory processes such as result from fractures or subcutaneous extravasations of blood. In this case the probable cause is the presence in the circulation of fibrin ferment set free at the site of injury. That fibrin ferment is capable of producing fever has been shown experimentally in animals, and in these the phenomena which follow have been found to correspond closely with those observed after the injection of toxins.

The most prominent and most constant of the constitutional signs of inflammation is a raised temperature, slight and transient in cases where the local process is aseptic, more marked and more lasting where a bacterial invasion has taken place. With this the pulse rises and is full and bounding; the respirations also become increased in frequency. The patient complains of headache, loss of appetite, and thirst; the skin is hot and dry, the tongue white and coated, the breath foul, and constipation is present, the motions when passed being unduly offensive. The urine is of high specific gravity, containing an excess of uric acid and urates, and in many cases albumin may be detected. If the inflammation continue, the general strength of the patient is seriously tried; he becomes exhausted and emaciated. The complexion grows sallow, and a varying degree of anæmia results. Delirium may ensue, and may usher in a fatal termination.

While such are the characteristic phenomena to be observed, it may be pointed out that two types of fever may be recognized—the *sthenic* and the *asthenic*. In the former the signs are those enumerated, and the term "sthenic" may fairly be employed when they are well marked. At times, however, owing to a particularly virulent form of infection, or consequent upon a prolonged duration of the inflammatory process, or, in other cases, as a result of an enfeebled and poorly resisting constitution, the signs are modified. The emaciation and exhaustion are more pronounced; the pulse-rate is very high, but the pulse is feeble and easily compressible; the temperature is higher. Anæmia is marked, the tongue is brown and dry, the teeth are covered with sordes, and a low muttering delirium ensues, to be contrasted with the restless or raving delirium of the sthenic type. Owing to the occurrence of this type of fever in the later stages of typhoid, it is often spoken of as "the typhoid state."

The constitutional signs of inflammation having been thus reviewed, the **causes** of these signs will now be considered. The regulation of the temperature is dependent upon a heat-regulating centre in the medulla, which maintains an equilibrium between the heat produced by tissue metabolism in, more especially, the voluntary muscles and great viscera, and that lost from the skin by radiation and perspiration, and

from the lungs by respiration. The occurrence of pyrexia is therefore an indication of either increased heat production or diminished heat loss. That the former suggestion is the only tenable one may be surmised from the obvious evidences of increased metabolism given by the wasting of fatty and muscular tissues, and the increase of urea and urates in the urine, and has been conclusively shown to be so by calorimetric observations in animals.

It is generally held that the increased heat production is not due to direct action of the circulating toxins or other pyrogenetic substance on the tissues, but rather to the derangement by them of the heat-regulating centre. The other phenomena observed in fever may be explained by the action of the toxic substances in the blood on the cells of the organs through which it circulates; thus changes are found, and may be demonstrated microscopically, in the cells of the heart muscle, of the kidney, and of the liver and other secreting glands of the digestive system.

Terminations of inflammation.—When the inflammation has not been severe or prolonged in character, the exudate may disappear, the blood-flow through the inflamed tissues be restored, and the vessels return to the normal. In such a case *resolution* is said to have taken place. In other cases the inflammatory action progresses; the continued action of the bacteria causes degeneration and death of the cells in the inflamed tissues and in the exudate, and so pus is formed. The second termination of inflammation is thus in *suppuration* Again, when inflammation is of longer standing, the tissues of the part become replaced to a greater or lesser degree by a mass of cells such as are present in inflammatory exudates. This mass of cells does not become absorbed again into vessels and lymphatics, but remains, and, undergoing vascularization, forms granulation tissue This later undergoes further transformation into fibrous tissue, bone, etc, according to its site. Such changes are particularly likely to arise when the inflammation is of a less severe or subacute type, but may also be a subsequent stage in the acute process, the formation of granulation tissue with its sequel, fibrosis, continuing sluggishly and producing the condition of *chronic inflammation*. When a free surface of skin or mucous membrane is inflamed the process may terminate in *ulceration*. Lastly, when the causal agent of the inflammation is of an unusually virulent type, or when constitutional or local changes have lessened the resistance of the tissues, *gangrene* may occur. The immediate cause of this is deprivation of blood-supply due to extensive surrounding thrombosis, and such a termination is particularly likely to arise when the density of the inflamed tissues is such as to render it difficult for swelling to take place in response to exudation. This will cause the vessel to suffer

from the pressure of the exudate, and will precipitate thrombosis when slowing of the blood-stream or stasis is already present.

Local treatment.—The introduction of Bier's hyperæmic method as a routine treatment for all inflammation seemed at first sight to be so absolutely opposed to the old methods of treatment, in which the chief aim was stated to be to relieve the congestion, that it is advisable briefly to review the theory of the treatment of inflammation.

It is now generally recognized that inflammation is not in itself a harmful process. It is evidence of the existence of a harmful process in the shape of a bacterial invasion. Moreover, it is in large part the attempt on the part of the body to resist that invasion. Diminution of the severity of the inflammatory phenomena accompanies the victory of the tissues over the attack. This is not evidence that the body has overcome the inflammation, but that it has overcome the bacterial invasion which was the cause of the inflammation. The inflammation subsides when the defeat of the bacterial invasion removes the cause. It is therefore necessary to dismiss the idea that inflammation is in itself dangerous. It is a danger signal (Adami). Bier, indeed, in his hyperæmic treatment aims at increasing hyperæmia, and incidentally the swelling and redness which are the cardinal signs of inflammation; and his method of treatment has been very widely adopted, though perhaps less in this country than elsewhere. From time immemorial, however, it has been looked upon as the greatest indication, in treating inflammation, to reduce the local congestion. The clinical observation that allowing the arm to hang down when a finger is inflamed causes the pain to become intense and throbbing, whereas raising the arm gives immediate relief, has so overshadowed the discussion on inflammation that it has been sought to prove that any and every successful measure adopted in the treatment of inflammation has for its rationale the diminution of congestion. Heat, indeed, has been almost universally included in textbooks under the means of relieving congestion, and many theories have been advanced as to the way in which it does this. That heat diminishes congestion has always seemed to me to be an untenable hypothesis, and contrary to all experience. It cannot be denied that, except in cases of traumatism, heat is the means nearly always employed in the treatment of inflammation, to the exclusion of cold. So, if it be accepted that heat produces hyperæmia, it would seem that the production of hyperæmia has always been the most commonly adopted method of treating inflammation. Of recent years the statement that heat diminishes congestion has been disappearing from textbooks, and the experimental work of Schäffer has thrown light on the actual local effect of this method of treatment. The experiments

referred to were carried out on rabbits. Threads were buried in the tissues on the two sides, either sterile, treated with chemical irritants, or impregnated with organisms. Heat was applied on one side, the other being left as a control. Removal and histological investigation of the affected areas enabled comparison to be made between the treated and the untreated tissues. It was found that, on the side on which heat had been applied, there was an intense hyperæmia with dilatation of the arteries, a very considerable exudation of lymph and, to a large extent, a disappearance of the leucocytes which, on the untreated side, were massed round the focus of infection or irritation. If suppuration had already occurred the application of heat caused an increase of the fluid constituents of the pus and an increased tension in the abscess which favoured pointing along the lines of least resistance. If, after allowing some hours for its effect to develop, the implanted thread was removed and heat then applied, it was found that the area of cell infiltration which was present on the side of control had almost completely disappeared on the side treated. These effects explain the clinical observations which are matters of everyday knowledge. While recognizing that heat increases hyperæmia and forms, as a rule, the best method of treating acute inflammation, it must be acknowledged that incisions, scarifications, local and general blood-letting, and the administration of cardio-vascular depressants do undoubtedly relieve the local hyperæmia, congestion, and exudation; and, moreover, it cannot be controverted that each and all of these have important places in the treatment of inflammation.

The truth is that different cases need treatment on different lines, and this principle is to be recognized in the practice of the past and of the present. Adami divides cases of inflammation into three classes, as follows: (*a*) *Where the local reaction is adequate.* The ordinary aseptic healing of a wound, or the normal process of union of a fracture, are examples of this. (*b*) *Where the reaction is inadequate.* Bacterial invasions supply the cases of this class. Here it must be understood that the mere fact of much redness, swelling, and heat does not show adequate reaction. The increase in these signs is, on the contrary, evidence that the bacterial invasion is not being overcome. *It is to* these cases that heat is applied as a routine treatment, and it is for these in particular that Bier's method of inducing hyperæmia might be employed. The added hyperæmia induced by either of these methods will bring to the part the leucocytes and protective substances of the blood needed to resist the microbic invasion. (*c*) *Where the reaction is excessive.* In these cases, owing to the virulence of the causative organisms or to the deficient vitality of the tissues, consequent upon some constitutional debility, the vessels of the part are

paralysed, the exudation is excessive—the excess being of fluid and the leucocytes few in number—and the sluggish circulation, with widespread stasis, is threatening extensive destruction of the part. Such cases as these the surgeon treats by incision to relieve tension and allow the draining away of toxin-containing serum, and so to restore the circulation in the affected parts. Such excessive exudation is also found after traumatism, and these are the cases in which cold is employed. Its action is to diminish the extravasation of blood from the vessels and to lessen the exudation. The case here is different from that of a microbic invasion; for, whilst one would not say that exudation after, for instance, a sprain is useless, yet it is not desirable in the same sense as in the former condition.

The methods employed in the local treatment of acute inflammation will now be considered in detail.

Removal of the cause.—Since the presence of bacteria in the tissues is the most frequent cause of acute inflammation, it is clear that removal of the cause is seldom feasible. Occasionally, as in the case of a malignant pustule, early excision will cut short the disease. Generally speaking, little more can be done than to remove a foreign body or other source of irritation, should such exist.

Rest.—Mechanical and physiological rest must be secured. Splints, slings, and bandages are employed to this end, and in some cases the recumbent position is called for. It is advisable to raise the inflamed part, as there can be no doubt that pain is thereby diminished.

Heat.—The application of heat is the most generally employed method of treating inflammation. Aseptic or antiseptic fomentations are usually applied. They have the disadvantage that they lose heat very quickly, and from this point of view poultices are preferable. Since, however, poultices are incapable of efficient sterilization and are dirty in application, they must never be used for an open wound, nor in cases where incision is likely to become necessary.

Cold.—The application of cold is chiefly of service in limiting exudation and extravasation of blood after injury. In inflammatory affections due to bacterial invasions its use is doubtful. It is often employed in the early stages of deep-seated inflammatory foci. Any relief that it gives in these cases is probably due to its effect on the sensory-nerve terminals, which reflexly influences other nerve-cells at the same level in the cord. These cells control the blood-supply of the deeper parts; diminution of congestion is thus brought about, and consequent relief of pain. In superficial inflammations—cellulitis or erysipelas, for instance—relief of pain is undoubted, but no treatment is more calculated than is cold to produce widespread sloughing. Evaporating lotions, ice-bags, and Leiter's tubes are the usual methods of applying cold.

Scarification and incision.—These measures are employed where there is much swelling and tension in the part and a sluggish circulation calls attention to the danger of necrosis. The former measure is employed in inflammation of mucous membranes, a series of superficial cuts being made with the point of a scalpel over the affected part. Incisions are serviceable, more particularly in inflammation of dense cellular tissue and of the periosteum of bones. They should be planned with due regard to the anatomical structure of the part. Fomentations are subsequently applied to encourage the discharge.

Leeches and cupping are employed for the purpose of local blood-letting over a deep-seated inflammatory focus. The amount of blood removed by these means is so small that it can have no influence on the general blood-pressure. That the amount of blood passing through the deep parts is directly affected is inconceivable, since there is usually very little connexion between the superficial and the deep vascular supply. Any effect is probably of a reflex nervous origin, as in the case of cold.

Bier's hyperæmic treatment.—The rationale of this treatment may be briefly summarized thus: Inflammation is not in itself a disease, but a condition brought about by the attempt of the living body to repel a bacterial invasion or to combat the effects of a mechanical injury. The hyperæmia, which is the earliest and most pronounced sign of inflammation, is therefore a beneficent phenomenon, and the object of the treatment is to increase this hyperæmia.

General treatment.—The resistance to microbic invasion is not only a matter of local reaction. The body, as a whole, is concerned in the process. Leucocytes and protective substances—antitoxins, opsonin, lysins, etc.—which are essential to successful resistance are not formed locally alone, but in the body as a whole. It is important, therefore, not only to treat inflammation locally, but also to place the body generally in a condition to do its share in combating the inflammatory process. Rest and avoidance of fatigue are essential, and in the severer cases this entails confining the patient to bed. The diet should consist of such food as the patient can most readily digest. Milk and broths or meat extract are all that is necessary in the early stages A large amount of fluid may be allowed. It is comforting to the patient, who is always thirsty, and increasing, as it does, the secretion of the kidneys and the skin, it assists in the elimination of toxic products. A purge should always be given at the outset of the treatment, *and the bowels should be kept freely active throughout* Saline aperients, such as sulphate of magnesium, are the most useful. The action of the kidneys and of the skin is stimulated by the administration of diuretics and sudorifics. Stimu-

lants will be necessary in those cases in which the asthenic type of fever is present. Brandy, strychnine, and digitalis are the best. The administration of quinine and other antipyretics is called for when the fever is high, and, should hyperpyrexia supervene, cold packs and hydrotherapeutic measures will be necessary.

Serum- and vaccine-therapy.—Of late years attempts have been made to increase the antibacterial properties of the blood in treating inflammatory conditions. These measures are described elsewhere (p. 109 *et seq.*), and will therefore be but briefly touched upon. It is possible in animals, by repeated inoculation with doses of organisms, to develop a high power of resistance on the part of the animal to those organisms. The antibacterial powers that the animal has acquired lie in certain substances contained in the blood-serum, and it is this serum which is employed for inoculation into the human patient. Although in a few diseases, such as diphtheria and tetanus, the uses of antitoxic serums are undoubted, the therapeutic advantages of other antitoxic or of antibacterial serums are very questionable in the case of the organisms found in common surgical affections. Much more promising, and, I may say, of proved service, is the administration of vaccines, consisting of known numbers of dead organisms of the kind which are attacking the patient's tissues. The inoculation of a vaccine is followed by a rise in the amount of immune bodies (opsonins) in the blood-stream, and these act on the invading organisms in such a way as to render them more vulnerable to the attacks of and ingestion by the leucocytes of the patient

CHRONIC INFLAMMATION

Symptoms.—There is a swelling of the inflamed area, due in part to hyperæmia and exudation, in part to the vascularization of the cells of the exudate, and in part to fibrous tissue into which the latter is converted by processes described under Repair (p. 169 *et seq.*). When the fluid exudate is a marked feature there may be œdema, recognized by "pitting" of the inflamed part on pressure. Pain is very variable, and is dependent upon the extent to which the tissue changes involve pressure upon sensory nerves. The pain in chronic inflammation of bone is often very great, although of a dull aching nature, whereas chronic inflammation of the synovial membrane of a joint may exist as a painless affection Tenderness may, as a rule, be elicited by pressure, and there is more or less evidence of hyperæmia given by the increased temperature of the inflamed area. There is usually no redness, unless the skin itself be involved in the process, although a dusky tinge or the presence of enlarged superficial veins is not uncommon.

Local treatment.—**Removal of the cause** is, as in acute inflammation, the first aim of the surgeon. Foreign bodies, necrotic fragments of bone, and carious teeth are examples of removable causes of chronic inflammation. Certain constitutional causes such as gout and rheumatism are alluded to under General Treatment (*see* below). There still remain, however, the great majority of cases, in which chronic inflammation is the result of a bacterial invasion, and in these cases complete removal of the cause is seldom practicable.

Rest, both mechanical and physiological, is as essential as in acute cases, and the elevated position is of equal importance.

Counter-irritation is widely employed and is of proved service. The method of action is not clear. The benefits derived have been attributed to a reflex nervous influence, and more recently to the increased hyperæmia induced by its use [1] The chief methods of applying counter-irritation are painting with iodine, blisters, the cautery, and the seton.

Pressure is useful in that it limits the exudate which is often a prominent feature, and perhaps also mechanically assists in its removal. Pressure is applied by means of elastic bandages and of strapping. The commonly employed Scott's dressing is a combination of this method and the last.

Massage acts by favouring the absorption of exudate, through its mechanical action in emptying the lymphatics, and probably also by inducing hyperæmia and quickening the blood-flow.

Free incisions into areas of chronic inflammation are often of striking value. They enable the exudate to drain away, remove pressure from the vascular and lymphatic channels, and produce a condition of hyperæmia by the mechanical traumatic inflammation which follows their employment. Incisions are more especially useful in treating intractable chronic inflammatory processes affecting bone.

Bier's hyperæmic treatment is largely employed and is of great value.

General treatment.—All measures should be taken to place the patient in the best possible hygienic surroundings. Tubercle and syphilis are two of the most frequent causes of chronic inflammation, and their presence calls for appropriate constitutional treatment. Such conditions as gout and rheumatism need the usual remedies; and, finally, when the persistence of the inflammatory process is endangering the patient's life, more especially if recovery would leave a limb of doubtful use, the question of amputation must be considered.

[1] The oft-repeated theory that counter-irritation of a surface diminishes the congestion of the underlying parts has been shown experimentally to be erroneous. It has precisely the opposite effect.

REPAIR

By J. M. BEATTIE, M.A., M.D.

The processes concerned in the repair of wounds or injuries are clearly defined, and it therefore seems unnecessary to refer to the work, interesting though it is, which has led up to the views now generally accepted.

No definite line can be drawn between the processes of inflammation and those of repair. The destructive and the proliferative changes, which are characteristic of all inflammatory reactions, may go on side by side, and in any given case the one or the other may predominate; but the term **repair**, in its general acceptation, is confined to that series of reactions in which the proliferative changes are in excess, and by which the injured tissues are restored to a condition more or less approximating the normal.

These proliferative changes are best studied in the healing of a wound of the skin and subcutaneous tissues; but it should be clearly understood that wherever they occur the same series of reactions is seen, though the intensity of these may vary in individual cases.

In some the repair may be *direct*, and result from the proliferation of the fixed connective-tissue cells of the part—most of the reactive phenomena of inflammation being either entirely absent or present only in a minor degree. Usually, however, the injury to the tissues will have caused some degree of reaction, and, as a result, there will be dilatation of vessels, leucocyte emigration, transudation of lymph, etc., with the consequent deposit in the injured area of fibrin and other inflammatory products. In addition, there will be destruction of the tissues, partly from the injury itself and partly from the reactive phenomena. This damaged tissue and these inflammatory products must be removed or absorbed before the healing process can be effective.

Again, the situation in which the injury occurs will have some effect on the character of the reparative changes. Thus, the changes seen in the repair of an injury of bone will differ from those which occur in the repair of an injury of the skin and subcutaneous tissues, but it cannot be too strongly emphasized that these differences are dependent

solely on the situation and the nature of the tissue to be repaired, the fundamental phenomena being identical in both cases.

It will be convenient, therefore, to deal in the first place with the essential processes, such as are seen in the healing of an incised wound of the skin and subcutaneous tissues, and later to discuss the variations which occur in connexion with the repair of special tissues.

ESSENTIAL PROCESSES OF HEALING

1. **The healing process as seen in an incised wound of the skin and subcutaneous tissues,** where the wound is not thoroughly aseptic and where the surfaces are not accurately in apposition: **healing by second intention.**

During the first *twelve hours* the margins of the wound are red and slightly swollen, these changes being due to the dilatation of the minute vessels—an early result of the reactive phenomena—and to the infiltration of the tissues with inflammatory lymph which has exuded from these vessels. At the same time the surfaces become *glued together by blood and by the coagulated lymph. Leucocyte* emigration is also well marked at this stage, the leucocytes, mainly of the polymorphonuclear type, passing both into the lymph and into the tissues at the margins of the wound.

In *twenty-four hours* all these changes become more marked, and the endothelial cells lining the blood-vessels, as well as the fixed connective-issue corpuscles, show swelling and distinct proliferative changes In from *thirty to thirty-six* hours after the wound has been inflicted vascular buds are given off from the minute vessels at the periphery. These buds, which are conical in shape, consist at first of solid masses of protoplasm containing nuclei. This protoplasm segments into irregular masses, the nuclei undergo division, and thus are formed endothelial cells, each of which contains usually a single nucleus. The newly formed endothelial cells separate from one another, and so open up new channels continuous with the lumen of the vessel from which the bud originated. From the distal end of these buds, long, irregular, protoplasmic processes grow out into the coagulated lymph and blood, and there anastomose with one another. Eventually these protoplasmic processes, together with the branches which they give off, open up in the same manner as the parent bud from which they arose, and by this process there is formed in the coagulated lymph an irregular network of vascular channels, lined by endothelial cells and communicating with one another and with the original vessels of the part. This capillary network may be present within thirty-six hours, and abundant evidence may be seen of the swelling and the mitosis of the endothelium of the developing

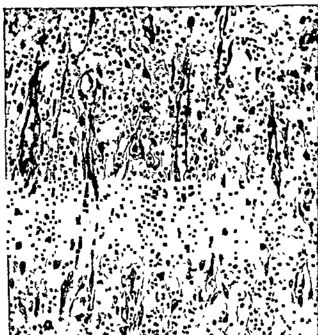


Fig 1 —Healing wound, showing granulation tissue, with thin-walled vessels, leucocytes, and proliferated connective-tissue cells × 200

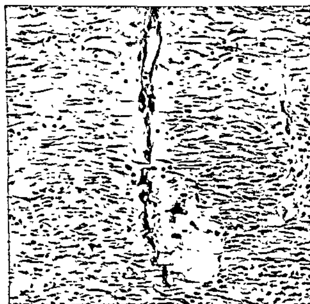
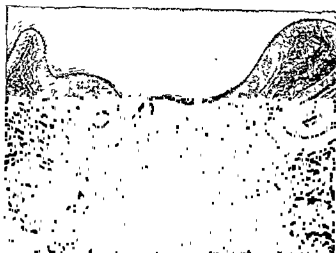


Fig 2 —Healing wound, showing new vessel with slight adventitial coat, and parallel layers of spindle-shaped cells × 200

PLATE 19.

(From Beattie and Dickson's "General Pathology")



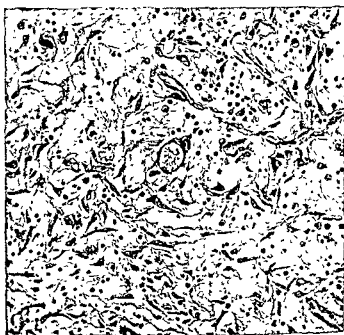


Fig. 2.—Granulation tissue from a healing wound, showing capillaries and the various kinds of cells. × 200.

PLATE 20.

(*From Beattie and Dickson's "General Pathology."*)

vessels. *Coincidently with its formation, gradual absorption and solution* of the inflammatory lymph takes place. At first the new vessels are extremely imperfect, having only an endothelial coat, but later an adventitia is developed, which arises as a result of the proliferation of the fixed connective-tissue cells of the part, these cells arranging themselves in lines parallel with the walls of the new capillaries (Plate 19, Fig. 1), thus forming a cellular supporting tissue which is more or less abundant in the capillary network. With the development of this supporting tissue there is a gradual absorption and disappearance of the inflammatory exudate. In this new tissue—the temporary granulation tissue—the vessels always remain thin-walled, and are composed merely of endothelium, or of endothelium with a few adventitial connective-tissue cells, and in consequence dilatation and rupture of them are common. This temporary granulation tissue appears mainly to have as its function the absorption of the inflammatory and other products, for when this work is completed the capillaries waste and disappear.

A new set of vessels is now being formed, especially in the deeper parts of the wound, and these gradually pass directly upwards towards the surface and are much more regular in their order of development and usually better supported than the primary set. They, too, arise from the pre-existing vessels by a process of budding similar to that seen in the formation of the primary capillary network. These vessels are well developed in forty-eight hours, and, at the same period, spindle-shaped cells are seen lying at right angles to the vessels; these cells —the fibroblasts—which have vesicular nuclei, abundant protoplasm, and long processes, soon form definite parallel layers (Plate 19, Fig. 2), which gradually extend upwards from the deeper to the more superficial parts of the wound, thus "sewing" together the two adjacent surfaces. They are formed mainly by a proliferation of the fixed connective-tissue cells of the part, though there is some evidence to show that they may also be formed from lymphocyte-like cells or from larger wandering mononuclears.

This new granulation tissue is the progenitor of scar tissue. In from three to five days definite fibrils are seen running parallel to the fibroblasts, and apparently formed by a transformation of the cytoplasm in the peripheral zone of the fibroblast. At the same time the second set of vascular loops show a thickening of their inner coat—a proliferative endarteritis—a filling-up of the lumen and a gradual shrinkage and disappearance. With the gradual increase in numbers of the fibrils, the cellular character of the tissue becomes less marked, and in three or four weeks both vessels and cells have almost entirely disappeared and have been replaced by dense white fibrous tissue—*scar tissue* (Plate 20, Fig. 1).

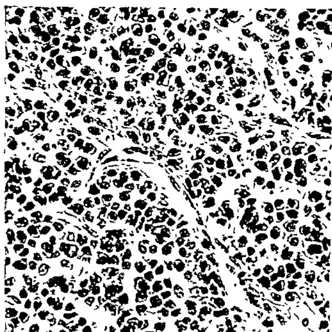


Fig 1.—A chronic inflammatory focus in the subcutaneous tissues, showing the great accumulation of lymphocyte-like cells (small-celled infiltration) × 400



Fig. 2—Fibroblasts in a healing wound of seven days × 400

PLATE 21.

or healing by first intention.—In these cases, as in a clean-cut operation wound, the healing may be quite complete in a few days. The changes which take place in such a case differ only quantitatively from those seen in healing by second intention. There is the same development of new vessels and the same proliferation of connective-tissue cells: a very thin layer of granulation tissue is formed, but this is identical in its structure with that seen in larger and more slowly healing wounds.

THE CELLS OF GRANULATION TISSUE

(Plate 20, Fig. 2)

Much discussion has taken place as to the origin and function of the various cells found in granulation tissue, and brief reference must be made to the subject for a proper understanding of present-day literature. The leucocytes of the blood are always present in varying numbers, in the majority of instances the polymorphonuclear forms being considerably in excess of the mononucleated ones; but in certain cases, and especially where the granulation tissue is infected with the organisms of tuberculosis or of syphilis, the lymphocytes, or at any rate basophile leucocytes resembling the lymphocytes, may constitute the vast proportion of the cells. In chronic inflammatory conditions, where the granulation tissue has developed slowly, it is common to find collections of small lymphocyte-like cells—the so-called small-celled infiltration. According to Maximow, these cells are mainly true lymphocytes which have migrated from the blood-vessels (Plate 21, Fig. 1), but there seems to be a considerable amount of evidence that many of them are derived from proliferation of the cells of pre-existing lymphoid tissue, while some, it is generally agreed, are adventitious cells of the blood-vessels and also proliferated pre-existing connective-tissue cells.

It is very commonly stated that the plasma cells, which many authors describe as occurring in connexion with chronic skin diseases and syphilis, are present in greater or less numbers in granulation tissue. Much confusion exists in regard to these cells (*see* p. 141), because of the uncertainty as to what different authors mean when they write about plasma cells. Many of the cells described as such are undoubtedly lymphocytes, while others are as certainly proliferated connective-tissue cells.

There can, we think, be little doubt that the endothelial cells lining lymph spaces and blood-vessels may be set free during the growth of granulation tissue, may wander from the vessels, and may act as very active phagocytes.

Clasmatocytes.—Spindle-shaped, branching cells, with irregular

nucleus and a cytoplasm containing metachromatic granules, are frequently seen, especially *in the later stages of granulation-tissue* formation. These cells, which were first described by Ranvier, are called clasmatocytes, and some authors regard the *mast cells* of Ehrlich as belonging to this class.

Giant cells.—Reference has already been made to the presence of these cells in granulation tissue (p. 172).

Fibroblasts.—These are the most important cells in granulation tissue, and are those finally concerned in the healing process, for from them the fibrous tissue is formed. They are, as has already been stated, derived mainly by proliferative changes from the pre-existing connective-tissue cells of the part, though there is evidence that some of them take origin from the lymphocyte-like and other mononucleated cells.

The fibroblasts, at first, are rounded or oval cells with a relatively large vesicular nucleus, but become elongated, spindle-shaped, or even stellate in appearance. They show fine fibrillæ projecting not only from their ends, but also passing directly through the substance of the cell-body. These fibrillæ gradually increase in size and number until *they almost completely replace the cell protoplasm, and eventually* the cell is represented by a nucleus, very much reduced in size, and a very small quantity of cytoplasm, the whole being surrounded by a bundle of fibrils (Plate 21, Fig. 2).

There are still differences of opinion as to whether these fine fibrils of white connective tissue are formed by a transformation in the cell protoplasm, or whether they are formed from the intercellular substance in direct apposition to the cell. The fibrils can be seen passing directly through the cells, and this seems to suggest formation from the cell protoplasm There is, however, considerable evidence that the intercellular substance, at any rate, shares in the process. The fibrils *arrange themselves more or less regularly in parallel lines*, become grouped into bundles, and so constitute the white connective-tissue fibres.

HEALING IN SPECIAL TISSUES

Epithelial cells. — The epithelial cells near the edges of the wound at first undergo degenerative changes, but in from ten to twelve hours proliferative changes are also seen. The cells become swollen, the chromatin of the nucleus becomes aggregated into a somewhat denser mass, and mitotic figures are found. New epithelial cells are *formed*, and these grow in layers parallel to the surface of the wound, gradually extending over the surface of the injured area. Many of these cells in the earlier stages of the healing process become œde-

matous and undergo degenerative changes, while others may become enclosed in the granulation tissue. As soon, however, as a supporting structure is constituted, the cells form a thin pellicle, which, if the wound is not too extensive, develops into a complete epithelial covering in from two to five days. In small, shallow, incised wounds the epithelial covering may be complete in forty-eight hours, whilst in large granulating surfaces months may be required unless the process is aided by skin-grafting. In healthy wounds a thin bluish-white line is seen at the edges, and on microscopical examination this is observed to be the new epithelium—at first, it may be, only a few cells in thickness. It is more or less firmly adherent to the surface, but can be rubbed off by even moderately rough treatment during the application or removal of dressings As the healing process advances, the layers of epithelial cells increase in number, the cells towards the surface become flattened and cornified; whilst those in the deeper layers are rounded, oval, or spindle-shaped, and it may be difficult to distinguish some of them from the fibroblasts of the granulation tissue on which they rest. The cells at the growing margin of the epithelium are often very irregular in shape, and may be separated from one another by the leucocytes of the exudate. When the covering is complete the exudation ceases and the proliferative changes in the deeper layers of the epithelium become very active, the degenerative ones being now absent

Skin-grafting.—This subject will be dealt with elsewhere, and here it is only necessary to discuss the reactive phenomena which follow the transplantation of the epithelial cells—the phenomena which are concerned in the healing process.

In from twenty-four to thirty-six hours the fragments of epithelium become firmly adherent to the surfaces of the granulations, and in forty-eight hours the pale-bluish line of newly formed epithelium can be seen This new epithelium, spreading from different centres, soon coalesces, and so large areas of granulation tissue may become completely covered in a few days. Microscopical examination shows that the adhesion of the grafts is brought about by the exudation of fibrin between them and the tissue on which they are placed. Usually the growth of the epithelium is from the more active cells of the deeper layers, the more superficial cells degenerating and being cast off. The definite papillary structure of the new epithelium may not be marked for several months.

HEALING IN NON-VASCULAR TISSUES

1. **Repair of wounds of the cornea.**—If the wound involves only the superficial epithelial layers, repair takes places by a proliferation of the cells at the margin of the wound, the condition being quite

analogous to the repair of epithelium in any other situation. In from twenty-four to forty-eight hours the new epithelium may have formed a complete covering.

If the wound is deeper and involves the fibrous-tissue lamellæ, marked proliferative changes are seen in the corneal corpuscles. These act as fibroblasts and send their processes into the lymph which has temporarily glued the surfaces together. The cells are arranged parallel with the lamellæ; and by them, without the intervention of vascular proliferation, the union of the surfaces is brought about. The anterior epithelial layer also proliferates, and usually overlaps the edges of the wound for a certain distance, forming a kind of plug in its upper part. In some cases the polymorphonuclear cells may have wandered to the site of injury, and may be found in the lymph or between the epithelial cells or the corneal corpuscles.

If the wound has reached the anterior chamber, the inner layer of epithelium also proliferates, and in three or four days the wound is filled with a mass of connective tissue, derived from the proliferated corneal corpuscles, and covered on each side by several layers of epithelium. In from six to eight days the superficial epithelium and Descemet's membrane are completely restored, and the new connective tissue has become more definitely fibrous, whilst in ten days to a fortnight the connective-tissue fibrillæ are well formed, and an opaque scar is the only sign of the original wound If the wound becomes infected, more extensive reparative changes are seen; leucocyte emigration from the conjunctival or episcleral vessels is a marked feature, and in the healing process new vessels grow in from the sclerotic and pass right up to the corneal wound. Granulation tissue similar to that which occurs constantly in vascular tissues is formed; purulent exudate may appear in the anterior chamber; and the iris frequently becomes adherent to the corneal surface, or it may even become entangled in the wound. Fibrous-tissue union is eventually formed, and the scar produced may be large and very opaque.

2. **Repair of cartilage.**—Wounds in cartilage usually heal very slowly and very imperfectly. A clean-cut, incised wound which is aseptic may heal by direct union of the opposing surfaces of the cartilage without manifesting any of the usual reactive phenomena of inflammation

Union, however, of large wounds is always by connective tissue, this being derived by proliferation from the perichondrium. Even this method of union may take several weeks or months before it is complete Small islets of cartilage are sometimes found in this connective tissue, and there seems little doubt that the fibrous tissue formed in the healing process may become transformed into cartilage, though this metaplasia is generally very incomplete.

Evidence of actual proliferation of the cartilage cells at the edges of the wound can sometimes be observed.

REPAIR OF ELASTIC TISSUE

The re-formation of elastic tissue is always imperfect, but new fibres are formed in the healing of wounds in situations in which elastic tissue is normally present. Fine fibrillæ can be seen projecting from the older strands at the edges of the wound, but it has not been satisfactorily demonstrated whether these fibres are new formations from the bodies of cells or whether they are merely outgrowths from the old fibres. Milne, dealing with the healing of wounds in the liver, states that "in certain areas a re-formation of elastic tissue has occurred, as there are far more elastic fibres than could possibly be derived from any mechanical aggregation or transposition of normal structures, further, they do not present the appearances of degeneration products. From six weeks till two months this patchy distribution of elastic tissue is maintained, but its elements have extended farther and are somewhat coarser. In incisions of three to four months' duration, although there still are large areas of connective tissue containing no elastic structure, yet there has also been a very extensive deposition of elastic tissue which intersects the fibrous strands through very widely distributed areas"

Further, he states that "a very considerable new formation of elastic tissue takes place in the liver The new formation always occurs in greater proportion in the fibrous-tissue healing of wounds which have always been aseptic, or in the reparative processes round necrotic areas, than in the repair of those which have been of an infective type The new elastic formation appears to be derived from some pre-existing focus"

Dawson says that "the elastic fibres found in the granulation tissue in wounds arise from a dissociation into fibrils of the pre-existing fibres. This is brought about by the exudation and the cell infiltration." This splitting up is apparently only a preliminary stage to atrophy and solution

The first new fibres arise, according to this author, as lateral projections from the pre-existing fibres at the borders of the wound, these new fibres running parallel with the connective-tissue cells and breaking up into branches which encircle the cells. He, however, points out that in scar tissue the very close relationship of the fibres to the cells, and the fact that the more delicate ones are in contact with the cell-border, whilst the thicker ones are farther out from the cell, certainly suggest a definite formation of fibres from the cells. The arrangement of the elastic tissue in walls of thickened arteries is also strongly suggestive of this latter view.

REPAIR IN FATTY TISSUE

During the processes of healing, much of the fatty tissue becomes transformed into mucoid or myxomatous tissue, though many of the fat cells may remain unaltered in the wound for a considerable time. At certain areas there are always to be seen collections of lymphocyte-like cells—the lymphocytes and plasma cells of some authors, or the polyblasts of Maximow. We think it probable that some of these cells may become transformed into fat cells. Maximow holds that of his polyblasts the clasmatocyte-like cells and the adventitious cells are the ones which are more particularly transformed into fat cells.

REPAIR OF MUSCULAR TISSUE

Unstriated muscle.—Though regeneration of this type of muscle by division of pre-existing muscle cells must be *admitted*, and though *in certain areas—e g. in the middle coat of arteries in healing wounds—the formation of new muscle-fibres is considerable, yet, as a general rule in wounds, the healing is almost entirely accomplished by connective tissue. Multiplication of muscle-fibres is seen in enlargements of the uterus or in hypertrophy of the muscular tissue of the stomach or intestine; but recent work seems to show that this new formation is comparatively unimportant, the enlargement being mainly a true hypertrophy of the individual fibres.*

Heart muscle.—Again, there seems no doubt that though the muscle-fibres may undergo definite proliferation, the nuclei of the cells showing evidence of mitotic division, yet healing is always brought about by the formation of fibrous tissue.

Striated muscle.—In clean-cut and small incised wounds, or in cases where only a small portion of muscular tissue is destroyed, there seems to be complete regeneration of the muscle; at any rate, it is impossible to make out, even microscopically, any evidence of the original injury. Where, however, larger amounts of muscle are injured or destroyed, union always takes place by fibrous tissue (Plate 22, Fig 1), though there is usually some evidence of muscular regeneration. Though the healing is thus anatomatically imperfect, it may be functionally good. If, however, the original wound has been extensive, there is very commonly contraction of the scar tissue, and contractures and deformities may result. Microscopical examination shows that degenerative changes are very marked in the muscle at the edges of the wound, and that the muscle-fibres become *surrounded by granulation tissue. The sarcolemma nuclei undergo definite and often very marked proliferative changes; the new cells thus produced are phagocytic,* and contain the remains *of the muscle substance.* Here and there among these cells may

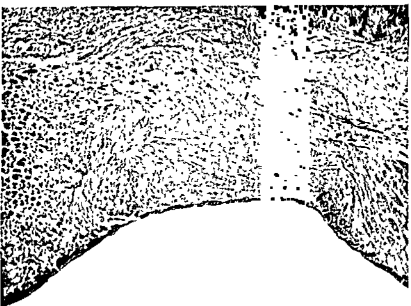


Fig. 1.—Wound of 21 days. Zones of degeneration and cellular regression replaced by cicatricial tissue. Zone of possible regeneration on either side containing ribbon form elements and spindle-shaped elements × 33. (*Dr James W Dawson, "Journal of Pathology and Bacteriology.*")

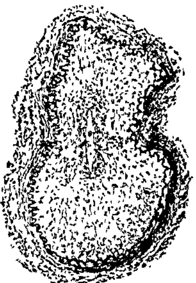


Fig. 2.—Organization in a thrombus, producing an almost complete obliteration of the artery.

PLATE 22.

be seen one which has apparently surrounded itself with sarcoplasm, suggesting an attempt at re-formation; whilst at other parts leucocytes, red blood-corpuscles, and other cells which have penetrated into the sarcolemma sheaths are seen.

Around the degenerating muscle-fibres there is, according to Dawson, a very active proliferation of the cells of the endomysium and of the capillary endothelium, and thus the tubes filled with cells which replace the degenerated muscle-fibres are surrounded by a meshwork of branching fibroblasts and numerous young blood-vessels.

Multinucleated masses of protoplasm are also seen, formed apparently by division of the nuclei of the cells of the sarcolemma without *division of the cytoplasm. These are regarded as muscle giant cells*, and they are intensely phagocytic to the muscle substance and also to other cells. The muscle-fibres in which degeneration is not so marked frequently show multinucleated, swollen ends, and it may be difficult to distinguish those from the muscle giant cells Dawson states that the end stumps can be recognized as elements of regeneration, and must be regarded as the muscle "buds" of Neumann Again, in certain parts of the wound he finds muscle-fibres dissociated into fibrils. This fissuring has in many cases every sign of a degenerative splitting-up of the fibre into its constituent fibrils. From other fibres, however, either from the sides or from the ends, long, narrow, spindle-shaped portions with elongated nuclei break off. In the surrounding tissue can be traced all transitions from these to long ribbon forms with many nuclei, which later become new muscle-fibres. These new muscle-fibres, however, seem comparatively unimportant functionally, and muscularization of a scar can only take place to a very limited extent. With increasing condensation of the scar tissue even these new muscle-fibres to a great extent atrophy.

REPAIR IN TENDONS

If the cut ends of a tendon are brought into strict apposition, direct union seems possible, and the healing is perfect, both anatomically and functionally

If the apposition is less perfect, a mass of granulation tissue will form between the separated ends. The cells of this are largely derived from the connective-tissue sheath of the tendon, the cells of this sheath showing definite proliferative changes in forty-eight hours. This granulation tissue becomes gradually less cellular; eventually a dense connective-tissue scar unites the two ends The true tendon cells also give evidence of proliferation, but at a much later period (four or five days) than the cells of the peritendinous connective-tissue. The scar tissue gradually contracts and becomes so dense that it is difficult to distinguish it from the original structure of the tendon. With

this contraction there is usually absorption of the surplus tissue which has been formed during the healing; and in this way the tendon may become quite free in its sheath. Sometimes, and especially if the wound has been septic, dense adhesions may be left between the tendon and its sheath, and thus serious interference with movement may occur. The time required for complete healing of a tendon varies. If strictly aseptic, two or three weeks may suffice, but if sepsis occurs there may be considerable delay.

REPAIR OF BONE

In simple fracture of bone there is either separation or laceration of the periosteum, and there is always more or less blood extravasation, the blood accumulating between the fractured ends. Within forty-eight hours the endothelial cells of the blood-vessels become swollen, and leucocyte emigration is well marked. Both in and around the blood-clot these leucocytes, together with cells which have been derived by proliferation from the periosteum, are found. At the same time newly formed vessels, derived from the pre-existing vessels of the periosteum, are seen passing into this new cellular tissue. Thus is produced a mass of granulation tissue which unites the two ends of the fractured bone and also forms under the periosteum a sheath which encircles the bone In this granulation tissue the cells are either spindle or very irregular in shape, and amongst them are a greater or lesser number of larger cells with numerous nuclei, often collected near the centre and resembling the osteoblasts of normal bone-formation. The cells lie in a matrix which at parts is homogeneous in structure and at other parts more or less fibrous. In four or five days the matrix become denser in structure, and the cellular character is lessened. This "osteoid" tissue, as it is called, becomes ultimately changed to bone, the ossification starting in the deeper layers and in the bony trabeculæ which are being formed in continuation with the outer layers of the original bone. Side by side with this new formation, absorption and modelling go on, in fact, the changes which take place during ossification are exactly similar to those seen during the normal processes of bone-formation

By successive deposits, large masses of this new bone—**callus**—are formed. Part of this becomes an ensheathing mass; part of it is found in the medullary canal (*internal callus*); and the smallest part, if the apposition of the bones has been well maintained, forms an *intermediate callus*, uniting the two broken fragments. During this formation of callus it has been shown that there is always more or less cartilage formed, and in this cartilage ossification eventually occurs.

The amount of callus produced is very variable, and depends on the condition of the bone at the site of fracture, on the size of the

bone, and on the nature of the injury. In fracture of the shafts of long bones the amount of callus formed is considerable, whereas in fracture of the cranial bones very little callus can be detected. Repair of *fractures of the epiphysial ends* of bones is usually unaccompanied by much callus Where the ends of the bones are not accurately in apposition there may be a considerable amount of callus, and in some cases the proportion of fibrous tissue to bone is so excessive that bony union is prevented

Compound fractures heal in the same manner as that described, but if infection of the wound has taken place the union may be considerably delayed, and not uncommonly necrosis of portions of the bone may occur.

In all forms of bony union the callus which is formed is usually more abundant than is necessary for the purposes of repair; but this excess is gradually absorbed. It is generally agreed that the absorption is brought about by large multinucleated cells, known as osteoclasts, though some authors regard the absorption as an atrophic or regressive change which takes place quite independently of these large multinucleated cells.

In the closing of cavities in bone—e.g trephine wounds—the replaced bone acts merely as a scaffold, and as the granulation tissue or osteoid tissue gradually grows into it from the periosteum and from the bone at the edges of the wound, it is slowly absorbed. The healing process is thus identical with that described for fractures.

HEALING IN VESSELS

The processes which take place are exactly alike, whether the wound be a small punctured one, or one in which the vessel is completely severed. In the latter case the hæmorrhage may be stopped by the retraction of the ends of the vessel causing a narrowing of its lumen, by the curled-up inner layers forming, as it were, a plug in the lumen, or artificially by pressure. Thrombosis in all cases is the first stage in repair. This thrombus, which is formed at first by an aggregation of blood-platelets, to which red blood-corpuscles, leucocytes, and fibrin are added later, may be very small, or it may occupy a varying length of the lumen of the vessel. The endothelial lining of the vessels undergoes proliferative changes, and may grow over the thrombus, isolating it from the general lumen of the vessel. If the thrombus is small and parietal, it may become completely covered by this endothelial growth and the lumen of the vessel be again made quite patent. Some authorities maintain that the endothelium grows into the clot and is actually the *progenitor of the fibrous tissue by which the* thrombus is eventually replaced. With this view I cannot agree.

The organization of the thrombus *is brought about exactly in the same manner as the healing in an incised wound. After a few days there* is an acute proliferation of the connective-tissue cells of the intima, and also, it may be, of the media; young capillary loops are formed, and these can be traced to the vasa vasorum, from which they undoubtedly arise. Thus there is formed a cellular granulation tissue which *brings about absorption of the blood-clot (Plate 22, Fig. 2),* and which *later becomes fibrous. The fibroblasts formed during the* process are smaller, and possess more branches, than those seen in the ordinary conditions of wound-healing. In this granulation tissue there is usually formed a considerable amount of elastic tissue.

If the thrombus is small, the healing may be so complete that the only evidence of it is a small fibrous scar. Where, however, it is in a *large vessel the process of vascularization is usually incomplete, and its more central part tends to degenerate—to become fatty* or even calcareous.

REPAIR OF NERVOUS TISSUE

In the **brain** and the **spinal cord** after injury there is a certain amount of proliferation of the various nerve-cells and -fibres, as evidenced by *mitosis; but these reparative changes are very imperfect.* The damaged tissue becomes softened and absorbed, and the filling-up of the defect is mainly brought about by a fibrous-tissue hyperplasia. This fibrous-tissue overgrowth is not a pronounced feature, and the cells which bring it about are derived mainly from the connective-tissue framework of the brain.

In experiments on animals this imperfect repair has been clearly demonstrated. Shortly after the wounds are inflicted, well-marked mitoses and other evidences of proliferative growth are seen both in the nerve-cells and in the connective-tissue framework; but in about ten days the mitoses are *not demonstrable, and there is distinct* evidence of destruction of the nerve elements, *with replacement of them by granulation tissue derived from the* connective tissue around the vessels.

Partial functional restoration has been recorded in a few cases of complete transverse lesion of the spinal cord after prompt union of the separated ends by suture. Though, therefore, *it must be admitted that restoration of nerve-fibres may take place,* still in the vast proportion of cases this new formation is very imperfect and does not usually supply any functional loss.

If the wound in the brain becomes infected, a hernia cerebri *is* formed, composed of granulation tissue containing *necrotic nerve-cells* and -fibres.

In **peripheral nerves,** however, the reparative processes are

definite. If the continuity of the nerve is interrupted, secondary degeneration occurs throughout the entire peripheral part, which has been severed from its trophic nerve-cells. The myelin breaks up into droplets and the axis-cylinders disintegrate. The nuclei of the neurilemma undergo proliferation. Following the degeneration, if the continuity of the parts be preserved, in favourable circumstances repair or regeneration, complete or incomplete, may occur. As to the method by which regeneration is brought about, there is still some uncertainty, different views being held as to whether the repair starts from the distal end of the central or upper portion, or from the proximal end of the peripheral part. For convenience, we shall speak of the former as the "central" and the latter as the "peripheral" end of the divided or injured nerve.

According to those who accept the central theory, the reparative process starts from the cut end of the proximal or central portion of the severed nerve. Either the original nerve-fibres, they maintain, grow downwards into the peripheral segment; or a number of young axis-cylinders are formed by division of each original axis-cylinder at the first node of Ranvier above the point of injury. These young axis-cylinders grow downwards into the original neurilemma sheaths, or fresh neurilemma sheaths may be formed from the proliferated neurilemma nuclei. This corresponds practically with the embryonic method of development, where the axis-cylinder grows directly downwards from a ganglion cell.

The second or peripheral theory has received the support of several workers on the subject, including Kennedy, Ballance, and Purves Stewart. Stated very briefly, the view which they maintain is that the peripheral segment of a divided nerve degenerates completely. This degeneration begins in a few hours after the injury, and is nearly complete in from three to four weeks. In the old sheath, neurilemma cells proliferate, become arranged in regular columns, and act as neuroblasts or nerve formative cells. While the degeneration is active, these cells of the sheath of Schwann show proliferative changes, and may be found between the myelin drops. They act as phagocytes to the myelin and to the axis-cylinders. Close to the nucleus of the neuroblast, a young, somewhat wavy axis-cylinder is developed, which soon becomes separated from the nucleus. Round this axis-cylinder a delicate myelin sheath is formed, the remaining neuroblasts *forming the new neurilemma sheath*. The young axis-cylinders join end to end to form more or less continuous chains, but do not undergo full development until they have become united to the central end of the nerve. These observers further state that the existing axis-cylinders at the central end play an entirely passive part until they become joined to the new peripherally formed fibres

Fleming, who supports this peripheral theory, maintains, however, that, in addition, new axis-cylinders are formed, at the central end of the divided nerve, from the old axis-cylinders.

That the central ends of the old axis-cylinders swell and give off a number of much finer fibres seems to us definitely proved. These extend through the cells which line and occupy the sheath of Schwann, and apparently join either with the old fibres, if these are not too far distant, or with the new fibres which have been formed from the neuroblasts as described above. Divided nerves—e.g. those occurring in amputations—may at their ends show some proliferation of the fibres, but the thickenings which occur so frequently on them—the so-called neuromas—are usually masses of granulation tissue entangling the nerve-fibres.

For complete restoration of the physiological function of a divided nerve, at least three or four months will be required. Sensation is restored before the power of movement of the muscles is affected. This is probably in part due to the fact that the function of the muscle which has been lost through the degenerative changes following the nerve injury takes some time to return even after the nerve healing is complete.

REPAIR OF WOUNDS IN THE HOLLOW VISCERA

Wounds of the **stomach** and **intestine** are frequently complicated by escape of the contents into the peritoneal cavity and the production of a localized or a wide-spreading peritonitis. If, however, there is no escape of the contents, and especially if the peritoneal surfaces become inverted and opposed to one another—as in suturing in operations on the intestinal tract—rapid union takes place, and in a few hours there may be definite adhesion between the serous surfaces.

Microscopical examination shows that this "gluing together" is brought about by fibrin and leucocytes which have accumulated as a thin layer between the apposed surfaces. The endothelial cells of the peritoneal covering swell and may become oval or cylindrical in form. Organization of the fibrinous layer takes place, and the granulation tissue formed becomes converted into a fibrous-tissue scar. The endothelial covering is restored by a growth from the pre-existing endothelial cells.

On microscopical examination some mitosis of the muscle-fibres is usually seen, but formation of new muscle-fibres takes place, if at all, only to a very slight extent. Restoration of the mucous membrane is brought about from growth at the margins of the wound—even the glands may be completely restored.

If the wounds are very extensive there may be a considerable



Fig. 1.—Repair in liver, two months after injury, showing replacement of damaged area by *granulation tissue*. × 60

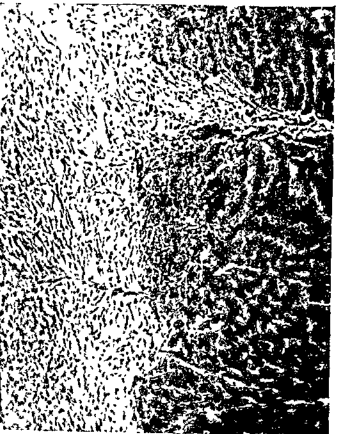


Fig. 2.—Granulation tissue in the liver, replacing liver cells in an injured area. × 100.

PLATE 23.

amount of cicatricial contraction of the scar tissue, and stenosis, more or less severe, may result.

Repair in the **gall-bladder** and the **urinary bladder** and **ureters** is brought about by the same processes as those concerned in repair of the stomach and the intestine. Complete union may have taken place in from ten to fourteen days.

REPAIR IN THE SOLID VISCERA

Liver.—In young animals one-half or three-fourths of the liver can be removed, and definite regeneration takes place, the liver eventually being restored to its normal size. In the human subject such extensive repair is probably not possible, but there is abundant evidence that extensive regeneration may take place. This new formation of liver tissue is particularly seen in cases in which there has been widespread destruction—e.g. in cirrhosis, in subacute yellow atrophy, in chronic venous congestion, in cancer, etc. The new areas are generally composed of large or somewhat irregularly shaped cells, closely packed together and very often presenting double nuclei. According to Milne, this regeneration results from a proliferation of the liver cells directly, and with no transition in type of cell; and, further, this regenerative capacity is specially manifested in those cells which occupy the outer zones of the lobules. The multiplication of the liver cell is usually by direct division, though karyomitotic division sometimes occurs.

It is generally held that in this reparative process the bile-duct and the interstitial connective tissue also proliferate. According to Milne, the numerous "bile-duct-like" structures which are seen in connexion with destructive and reparative conditions in the liver, especially in those cases in [illegible]
not really new ducts, but " [illegible]
bile-conducting channels wh[illegible]
interlobular bile-ducts." He further states that when these structures become exposed in granulation tissue, their lining cells swell and become more evident, and assume a definitely cubical shape. Experimentally, these ducts become conspicuously evident in about four or five days as tubes lined by a somewhat thin, flattened epithelium; but in ten days the epithelium is definitely cubical in shape. These lining cells sometimes multiply locally, but they never reproduce cells with any close resemblance to liver cells

In wounds of, or incisions into, the liver, especially if these are not extensive, healing takes place by the formation of fibrous tissue, but even in these cases some regeneration of the liver tissue may be seen at the peripheral parts of the wound. (Plate 23)

Spleen.—Repair in the spleen is only observed after small tears or



Fig. 1—Repair in liver, two m   s a   [illegible] injury, showing replacement of damaged area by granulation tissue. × [illegible]

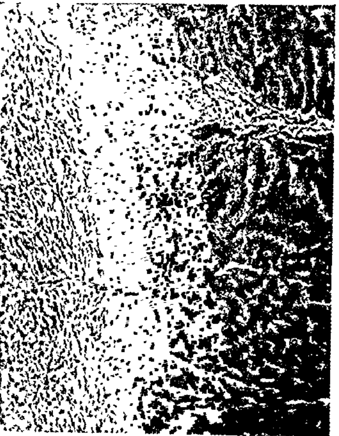


Fig. 2—Granulation tissue   , the liver, replacing liver cells in an injured area. × 100

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In wounds of, or incisions into, the liver, especially if these are not extensive, healing takes place by the formation of fibrous tissue, but even in these cases some regeneration of the liver tissue may be seen at the peripheral parts of the wound. (Plate 23)

Spleen.—Repair in the spleen is only observed after small tears or

wounds, larger wounds giving rise to rapidly fatal hæmorrhage. There appears to be no evidence, either experimentally or in cases observed in the human subject, that new splenic tissue is formed. The blood-clot which fills up the gap in the organ becomes organized. The granulation tissue which is formed becomes fibrous, contracts, and a connective-tissue scar is produced.

Kidney.—Wounds in the kidney heal by granulation. A clot of blood is formed between the cut surfaces, and into this leucocytes and other cells pass. New vessels are formed from the pre-existing vessels, and thus a layer of granulation tissue forms and unites the two cut surfaces. A fibrous-tissue scar is the final result of the healing process. Fibrous glomeruli can usually be seen in this scar, the fibrous tissue having invaded the kidney tissue lying adjacent to the wound. Apparently a certain amount of regeneration of the collecting tubules can take place, but the secreting tubules seem incapable of re-formation. There is generally necrosis of the cells of the tubes of this type, which are lying close to the wound, while those farther removed may show atrophic changes, the epithelium having undergone regressive changes with the production of a low, flat epithelium.

Repair after decapsulation.—Decapsulation as a method of treatment for chronic nephritis has been strongly recommended by various surgeons. Edebohls holds that a new capsule is formed, and that during its formation new vessels pass into the substance of the kidney and thus increase its blood supply. It is possible that in the early stage of the formation of this new capsule there may be an increased vascular supply to the superficial parts of the kidney; but later these vessels contract or become obliterated by fibrous-tissue overgrowth, and the new fibrous tissue extends into the kidney. From a pathological study of the condition there seems to me no doubt that repair takes place after decapsulation, but that the subsequent cicatricial tissue which is of necessity formed usually renders the procedure of no permanent value.

REPAIR OF THE UTERUS AND FALLOPIAN TUBES

Wounds of the muscular wall of the uterus and of the Fallopian tubes heal by the formation at first of granulation tissue, but at a later period there is certainly regeneration of muscle-fibres, and in small wounds it may be impossible in a few months to detect any evidence of a scar. In larger wounds, however, the fibrous-tissue scar is always evident.

The mucous membrane, after curetting, regenerates completely, the connective tissue and vessels being formed rapidly as granulation tissue, the glandular part being reproduced from remnants of the

glandular tissue left in the deep muscular layers. It is also possible that the regeneration of the glands of the endometrium may take place from small fragments of the mucous membrane which have not been removed.

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SUPPURATION

By Sir G. LENTHAL CHEATLE, K.C.B., C.V.O., F.R.C.S.

Definition.—Suppuration is the term applied to that process in which an external excitant and living tissues act upon one another to cause death of tissue, emigration of leucocytes, and exudation of serum When these things have occurred suppuration has taken place, and the fluid which collects in the centre of the lesion is called *pus.*

It may be said at once that the external excitant is practically always a micro-organism, and that suppuration may be one of the processes concerned in the attempt, on the part of the host, to establish that immunity upon which recovery ultimately depends.

Clinical types.—Suppuration may be acute, subacute, or chronic. An acute suppuration develops within about seven days, or less; a chronic suppuration deve'ops in one or more months; while a subacute suppuration matures in the intermediate periods. These are terms of clinical importance which indicate the degrees of intensity produced by the actions upon which depend the signs and symptoms of the disease; but they have also a bacteriological importance, for chronic suppurative conditions are very commonly found to be associated with the presence of *Bacillus tuberculosis,* or with organisms of the streptothrix group (actinomyces, etc.) The presence of these organisms in the pus in association with their well-known pathological changes is the only proof of their causal nature, for it is well established that organisms of the staphylococcal group, *B. coli,* etc., may produce chronic as well as acute suppurative lesions. It is therefore essential that a bacteriological examination be made of the pus or of the tissue walls of the suppurating focus. Although the identification of the micro-organism must always be the feature of first importance in diagnosis and prognosis in suppuration, the surgeon must be alert to observe the local and constitutional clinical changes, for these will help him to determine the probable resisting power of his patient, and to order treatment accordingly. Much discretion must be exercised in the estimation of the relative importance of clinical signs. The writer has seen multiple abscesses of such feeble intensity that they gave no hint that they were due

to *Streptococcus pyogenes* of such virulence as to cause the death of the patient.

Anatomical sites.—Suppuration may occur in pre-existing cavities, such as the pleural, pericardial, peritoneal, meningeal, synovial and bursal cavities; in the bony sinuses of the nasal and aural regions; and on mucous surfaces. It is common in the skin, in the subcutaneous tissues, cutaneous glands and hair-follicles, and around nails. In bone it may affect the subperiosteal tissues, the compact and cancellous tissues, and the medullary cavities. It may be a process superimposed upon other morbid conditions, e.g. biliary, renal, and vesical calculi, simple and malignant tumours and cysts. In such circumstances it must be looked upon as a complication of these conditions, though in some of them it is often of more importance than the pathological condition which it complicates.

Suppuration may also complicate an "ulcer," or, by inducing gangrene of the parts which cover subjacent suppuration, may be a direct cause of an ulcer. By preventing union of a wound by first intention, the subsequent ulcer would be caused directly by the process of suppuration.

Etiology.—Suppuration can occur only as a result of an external agent accidentally or experimentally introduced into the tissues of the living host. At present there is no evidence to prove definitely that alterations in the metabolism of cells or any products of autolysis can induce suppuration.

The *excitant* may be living or lifeless. Though it is the living excitants only with which one has to deal in ordinary clinical work, yet it is well to recognize that suppuration may be caused by lifeless ones. Chief among these are micro-organisms previously killed by heat at low temperature, products of micro-organisms, croton oil, pyrogallic acid, cantharides, carbolic acid, turpentine, and abrin. None of these agents can multiply in the body, but they may be carried from one part to another by the blood- or lymph-stream. Since the injection of serum has come into constant use it may be well to mention "Arthus phenomenon," one manifestation of which may be the development of an aseptic abscess in a guinea-pig which has been injected frequently with normal horse-serum.

The chief causes of suppuration induced by living excitants are micro-organisms, of which the most prominent will now be mentioned.

Micro-organisms which induce acute suppuration.—These are: *Staphylococcus pyogenes aureus. S. pyogenes albus. S. pyogenes citreus. Streptococcus pyogenes. Pneumococcus. Gonococcus. Bacillus coli communis. B. pyocyaneus. B. mallei. B. pestis. Meningococcus. B. influenzæ. M. tetragenus. B. pneumoniæ.*

The staphylococci and streptococci are the commonest causes of

acute suppuration in adults; these and pneumococci are commonest in children. In the skin and subcutaneous tissues, suppuration produced by pure streptococcus is not common, and when this micro-organism is found in pure culture in the lymphatic glands or in the subcutaneous tissues, careful investigation, in my experience, generally shows that the suppuration has *occurred during or after an attack* of erysipelas. The site of inoculation is an important factor in determining the kind of micro-organism which may be present; e.g. in *peritoneal suppuration* which is induced by appendicitis the *B. coli communis* is commonly found, whereas in suppuration in the pleural cavity in cases of pneumonia the pneumococcus usually is present. Pneumococcal peritonitis in children is more common in females. There is important evidence to show that the vagina is the pathway of infection.

Micro-organisms which induce chronic suppuration—The micro-organism which is most constantly found in chronic suppuration is *B. tuberculosis.* Chronic suppuration and tuberculous suppuration have become almost synonymous terms in spite of the fact that tuberculous disease is more a degenerative than a true suppurative process. *More typical chronic suppuration* may be *induced by B. typhosus, B. mallei,* and by the actinomyces and other streptotriches. Kocher and others have shown that the micro-organisms which usually induce acute or subacute suppuration may occasionally give rise to slowly formed semi-quiescent collections of pus. This form of chronic suppuration occurs more particularly in bones, and especially at their extremities.

Other micro-organisms are found more or less frequently in pus, but proof is still required that they are its exciting cause; under this head may be classed—*Spironema pallidum, B. anthracis,* and certain hyphal fungi, especially varieties of *Aspergillus* and *Trichophyton.*

How the micro-organisms of suppuration gain entrance.—Micro-organisms which cause suppuration gain entrance, in the majority of cases, if not in all, through a solution of continuity. Garré rubbed *virulent staphylococci on the surface of the skin,* and provoked foci of acute suppuration; but there can be little doubt that he made wounds and infected them. In large wounds the liability to infection is greater than in small ones, yet the *size is not of fundamental importance.* Slight suppuration may occur in a large wound; and intense suppuration, ending fatally, may be initiated by infection of a wound so small that it cannot be seen. Any article which causes the wound may carry on it the micro-organisms that induce suppuration, or they may gain admission at a period later in the wound's history.

It may be taken as a law that if suppuration should occur in a wound of which the skin edges have been brought together, and which

does not communicate with any septic focus, then the micro-organisms gained admission during the operation—even when the suppuration does not become evident until the lapse of three weeks or more. Where this occurs there is usually a history of rise of temperature, pain, or want of union, which affords ample evidence of early infection.

Factors upon which suppuration depends.—Suppuration, depends upon the definite adjustment of certain factors at the moment of inoculation, and upon the degrees in which these factors are adjusted depends all the subsequent course of events. Suppuration does not necessarily follow an inoculation of micro-organisms because they are capable of inducing that process. For instance, the inoculation of streptococcus may cause no visible change, or it may induce an area of hyperæmia, a local collection of serum, a collection of pus pyæmia, or even death in a few hours. I have seen many lesions develop which were induced by the presence of pneumococcus in pure culture, but in none of them was there any true suppuration. The factors which, to produce suppuration, must be definitely adjusted at the moment of inoculation are considered under two headings—(1) the micro-organism; (2) the host.

(1) Factors connected with the micro-organism. (*a*) *The kind of micro-organism*—It is not all pathogenetic micro-organisms that have the capacity to induce suppuration (*B. tetani*). Moreover, suppuration does not inevitably follow the inoculation of a culture which is known to be capable of inducing it under other circumstances. Perhaps the micro-organism which induces suppuration with the greatest degree of certainty is the staphylococcus. The inocu'ation of the streptococcus may be followed by a great variety of effects, as has just been mentioned.

(*b*) *Dose.*—The dose, i.e. the number of micro-organisms inoculated, is more important in the case of those whose virulence and variation of virulence are not very great. Although there is variation in the virulence in different strains of staphylococcus, yet there is not the great variation that is observed in streptococcus, hence the dose is a very important factor in the case of staphylococcus, and virulence may be a more important factor in streptococcus, but even in a streptococcus culture capable of inducing suppuration the dose must remain an important factor. The dose of staphylococci necessary to produce suppuration in rabbits was shown by Watson Cheyne to be 250 millions. Harman found that it required 500 millions of staphylococci to produce an acute abscess in rabbits, but that 50 millions were sufficient to cause the same result in dogs. My experience would suggest that these figures are excessive in the case of man; mankind appears to be more susceptible to staphylococcus infections than are the lower animals

(*c*) *Virulence.*—The virulence of a micro-organism is an important

factor in discussing its capability of causing suppuration. A large dose of a highly virulent micro-organism would probably kill a host without inducing a *suppurative process*, whereas a small dose of the same culture might cause an acute abscess and nothing more. But there is a degree of virulence in which it would seem impossible to inoculate a dose sufficiently small to avoid a fatal issue in a few hours; for instance, Marmorek and W. Bulloch showed that the virulence of a streptococcus can be so intensified by passing the culture through rabbits, that even half a millionth of a cubic centimetre caused death in seven hours. The degree of virulence of the inoculated micro-*organism influences the behaviour of the tissues of the host*, and the initiation and degree of suppuration depend greatly upon it, and the degree of virulence varies in the life-history of the micro-organism. It must not be inferred that a suppurative process stops because the virulence of the micro-organism grows less; that is not a fact. A man under the care of the late William Rose recovered from a diffuse suppuration of the thigh, and at the last operation that resulted in a recovery the *B. mallei* was as virulent to male guinea-pigs as it always was. *The recovery depended more than anything else upon* the man's acquired immunity.

(*d*) *Method of inoculation.*—It is possible to demonstrate that a dose of a micro-organism inoculated in mass behaves differently from the same dose inoculated in fine emulsion. I have convinced myself that a mass of staphylococci taken from the surface of a culture on agar and inoculated under the skin can induce suppuration at the seat of inoculation; but when the same dose from the same medium is *inoculated in fine emulsion, suppuration at the seat of inoculation* does not of necessity follow

(*e*) *Purity or mixture of infection* probably has an influence upon events in the host. When a staphylococcus is inoculated with another organism which is not capable of inducing suppuration, such as *B prodigiosus*, a smaller dose of staphylococcus appears to be capable of producing suppuration than when *B. prodigiosus* is absent. It is not possible to explain the fact. *B. prodigiosus* is not pathogenetic, except in very large dose. The combination of the two micro-organisms may increase slightly the virulence of the staphylococcus, or the presence of the comparatively small dose of *B. prodigiosus* may render the tissues of *the host more susceptible to the action of the* staphylococcus. At any rate, it is known that the action of other micro-organisms is modified by mixture of infection; for instance, *B. tetani* is more dangerous *when its infection is mixed with micro-organisms capable of* inducing suppuration, probably because *B. tetani*, being an anaerobic organism, only becomes active through a utilization of oxygen by the associated pyogenetic organisms.

(2) FACTORS CONNECTED WITH THE HOST. *Immunity and susceptibility*.—One host may be immune to a suppurative process to which another may be susceptible, although the same dose of the same micro-organism and of the same degree of virulence be inoculated. Age has an important influence upon the incidence of some suppurative processes. Infants are very susceptible to suppuration caused by the pneumococcus, to which adults are not so liable, similarly, the vaginal mucous membrane of a child is very susceptible to infection by the gonococcus as compared with that of the adult

It is a fact that some parts and tissues of the body are more immune to the suppurative process than others; that is to say, the immunity may be local. Suppuration does not occur in cartilage, and uncongenial soil is found in fibrous tissue, erectile tissue, and arterial tubes, except in aneurysm and infective embolism. The bactericidal power of blood is well known; suppuration may extend from a vessel wall into a thrombus, but it is commoner for an infected thrombus to be the starting-point of the suppurative process

Suppuration is especially frequent in the cutaneous and subcutaneous tissues, particularly at the back of the neck—a fact not altogether explained by the frequency with which these tissues may be inoculated. The same remark applies to the matrix of the nail (whitlow).

Certain micro-organisms are more prone to induce suppuration in certain tissues than in others For instance, the gonococcus is most active on the mucous membrane of the urethra, cervix uteri, and conjunctiva, less active on synovial and serous surfaces, and very slightly active in skin and subcutaneous tissue, lymphatic glands, and the adult vaginal mucous membrane. I have seen a streptococcal cutaneous erysipelas spreading from the hand to the tissues about the base of the neck, and producing suppuration only in the bursa covering the olecranon process and in the supraclavicular lymphatic glands The pus in these regions contained *Streptococcus pyogenes* in pure culture I saw an officer in the South African War with a small septic bullet-wound in the heel, from which cutaneous erysipelas spread upwards to the groin, yet the only part in which suppuration occurred was the prepatellar bursa, and in this streptococci were the only micro-organisms observed microscopically.

A person who has recovered from a suppurative process may enjoy, for a time, immunity from the specific micro-organism which induced the disease. The length of time which this active acquired immunity lasts varies with different micro-organisms. In dogs I found, experimentally, that the active acquired immunity after a staphylococcus suppuration was very temporary, lasting about fourteen days After a streptococcus infection, immunity may last about six weeks, and after

an attack of typhoid fever immunity may extend over several years.

Natural and acquired general immunity can both be diminished, and natural general susceptibility increased, by fatigue, starvation, alcoholism, exposure to cold or wet, by diseases such as diabetes and nephritis, and by injury.

Passive acquired immunity is induced by *injecting into a susceptible host the serum from an animal which has actively immunized itself by having suffered from the effects of the same micro-organism.* Unfortunately, it is at present difficult or impossible to apply this method of establishing immunity in treatment against the micro-organisms capable of inducing suppuration. Passive acquired immunity may be induced also by vaccines.

Local susceptibility can be induced by disease or injury, and a part injured before or after inoculation may be the focus of suppuration, although the micro-organisms were introduced elsewhere. War experience has added force to the rule that all dead tissues should be removed from a recently inflicted wound Suppuration is thereby thwarted or rendered less serious.

I have shown in another place that in some acute and chronic infective processes this local susceptibility must be related in some degree to the nervous control of a part, which allowed infection in the affected area and prevented it in adjoining areas It must be admitted that the neuro-vascular state must be an important factor in influencing the course of infective processes; but it cannot be imagined that changes in the neuro-vascular state can account for the selection of one nerve area and the escape of its immediate neighbour. Vascular anastomosis is too complete. Amongst other cases which I have collected that bear on this point is one in which the regions described by Henry Head as the nasal regions were attacked by erysipelas (streptococcus) which never spread to neighbouring areas. This extreme localization cannot have been due to neuro-vascular causes.

Dissemination.—Many micro-organisms are themselves motile, being possessors of flagella, but those without flagella seem to be equally liable to dissemination.

The pre-existing channels and cavities by which dissemination is facilitated are the blood- and lymph-vessels; the meningeal, pleural, peritoneal, synovial, and mucous cavities, the tendon sheaths and the bursæ communicating with them; the nasal and genito-urinary mucous membranes and their communications; and the ducts of glands.

The frequency of dissemination or generalization of micro-organisms is not generally appreciated. I have shown by experiments that,

even when an inoculation is manifested only by a local suppuration, the inoculated host passes through a general as well as a local infection. I found in one series of experiments that, in an animal killed five minutes after an inoculation of staphylococci into the subcutaneous tissue, the micro-organism could be stained in and cultivated from the liver, the heart and lungs. At the same time, the exact dose of the same culture of the micro-organism was inoculated into the same parts of a control animal which subsequently developed only an acute suppuration at the seat of inoculation. These experiments show that the body of the host was able to deal summarily with the disseminated micro-organisms, although an obvious effort was required to rid itself of the masses of them which were arrayed against it at the seat of inoculation.

The reader will see from these experiments two things:

1. Although only local change is obvious in suppuration, the patient has passed through the crisis of a general infection which occurred at the moment of inoculation. And during the process of suppuration a host is protecting himself against generalized bacteria, a few of which can be demonstrated in the blood, especially in the early stages, if a sufficient quantity (10 c.c.) be examined. Thus, in the early stages of pneumonia and typhoid fever the respective micro-organisms can be found without difficulty in the circulating blood

2. The patient, by the time suppuration has occurred, has already run the risks of acute septicæmia or of pyæmia, either of which might have occurred if the micro-organism had been possessed of greater virulence, or had been disseminated in larger dose, or if the host had been more susceptible.

It follows, therefore, that the effects of an infection inevitably depend on the balance between the contending powers at the moment of inoculation—viz. (1) the micro-organism, and (2) the host. Although the later course of the infection may be influenced by subsequent changes in the micro-organism and in the host, the actual degrees in which the powers of attack and defence are present at the moment of inoculation are the foundations upon which rest all the subsequent changes.

Clinical forms of acute suppuration.—An acute suppuration is exhibited clinically in one of two forms, *acute circumscribed abscess* and *acute diffuse suppuration*.

The acute diffuse suppuration is the more serious of the two, and while it lasts the limb or even the life of the patient may be in jeopardy. The process is more intense than in the acute circumscribed form. Apart from this, the pathology of acute circumscribed abscess and of acute diffuse suppuration is practically identical, and microscopical sections made from the margins of these lesions exhibit such similar changes that it is not always possible to state which of the two is under

observation. Hence, to avoid needless repetition, the pathology of these conditions will be described under the heading of acute circumscribed abscess, and when differences arise more closely associated with acute diffuse suppuration they will be indicated.

ACUTE CIRCUMSCRIBED ABSCESS

Definition.—Acute circumscribed abscess is the term applied to a localized, rapidly formed collection of pus in a cavity produced by the suppurative process.

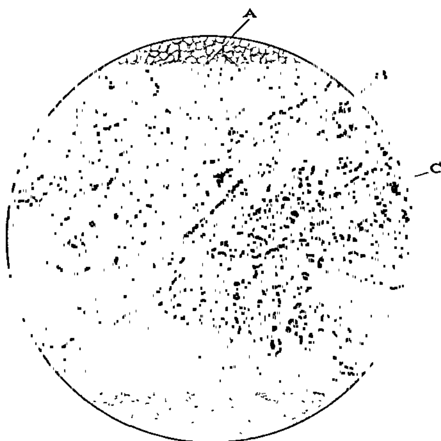
Pathological anatomy.—For the purpose of description the sequence of events in the development of an acute circumscribed abscess in the subcutaneous tissue will be dealt with under three heads:—

1. Entrance of micro-organisms and their effects in producing emigration of leucocytes, transudation of lymph, and death of tissue.
2. Proliferation of the neighbouring fibrous bands and connective tissue which normally connect and support the adipose tissue; this is commonly called encystment of the abscess
3. Rupture of the abscess.

1. The micro-organisms at once begin to multiply, and their products kill the tissues with which they come in contact At the end of the *first hour after inoculation* they are scattered diffusely among the tissues into which the inoculation was made Emigration of polynuclear leucocytes, transudation of lymph, and necrosis of the tissues are now evident. Around the margins of the living tissues leucocytes are collecting in considerable numbers, even at the end of the first hour; some have already penetrated the dead area and met their death; many of the immigrated leucocytes have incorporated a large number of the invading micro-organisms (phagocytosis).

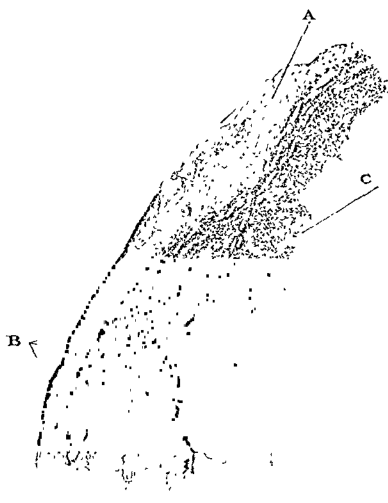
By the end of *twenty-four hours* both micro-organisms and leucocytes have increased enormously in number, and masses of micro-organisms are seen scattered among great crowds of leucocytes, many of which are evidently dead and degenerating (leucolysis), whilst phagocytosis has greatly increased. Mixed up with these are masses of necrotic tissue, and also areas of more resistant fibrous tissue which has not yet undergone death and liquefaction. At the margin of the abscess local connective-tissue cells begin to multiply; they are also seen in small numbers lying free among the leucocytes and micro-organisms at the edge of the lesion. Enormous numbers of micro-organisms are seen in the liquid content in the centre of the lesion.

In *forty-eight hours* all these processes have increased, and one remarkable change is to be noticed. Micro-organisms, when stained, can be seen (low power) forming a sinuous line around the margin of the lesion; under a high power they are seen to be lying between



Spreading infection (staphylococci) in subcutaneous tissue of guinea-pig, 48 hours after inoculation. A, Adipose tissue; B, the same infiltrated with polynuclear leucocytes and staphylococci; C, bundles of striated muscle being separated from each other by the same infiltrating process. × 50.

PLATE 24.



Subcutaneous tissue of guinea-pig, four days after infection with staphylococci. A, Hypertrophied band supporting connective tissue against which abscess has impinged; B, unorganized blood-vessels in middle layer of so-called abscess wall; C, abscess cavity. × 50.

PLATE 25.

newly formed connective-tissue cells and leucocytes that have collected there—the latter also incorporating many of them. This line of micro-organisms at the margin of the lesion is characteristic, and must be important; it can be stained throughout the whole subsequent course of the lesion. (Plate 21.) It seems to indicate the establishment on the part of the host of some degree of conquest.

At the end of the *fourth day* (Plate 25) the condition of things has become more definite. The micro-organisms around the edge of the lesion, but within the area of disease, are very evident, and the local connective tissue has been busily multiplying here, so that leucocytes, connective-tissue cells, and micro-organisms are collected in great numbers Newly formed capillaries can be seen within this marginal area, and are the main source of the hæmorrhage which occurs when an abscess bursts or is opened. Around the focus of disease the fibrous-tissue bands which normally support the blood-vessels, nerves, and adipose tissue are hypertrophied; their increase in size becomes less and less noticeable the farther away they are from the focus. From this stage onwards it is, in my experience, very difficult to demonstrate any micro-organism in any other part of the body than in the margin and centre of the abscess

By the *seventh day* (Plate 26) all these conditions are still more marked; but, although the abscess may be on the point of bursting, there are many parts of its margin which have no limiting fibrous tissue. Where fibrous-tissue wall exists, it seems as if the disease has extended to it accidentally rather than that the disease has been encircled intentionally by the fibrous wall. The increase in the amount of fibrous tissue may augment the degree of local immunity, but it cannot be said to account for the limitation of the disease, because of its frequent and complete interruption even when recovery is occurring.

The dead and liquefied tissues, the emigrated leucocytes, and the collection of serum constitute PUS. Pus can be recognized at the end of twenty-four hours in the centre of the lesion. When collected and examined it is a thick, opaque fluid, white to lightish-yellow in colour, fatty or greasy to touch; it often possesses a peculiar animal odour, and the reaction is usually alkaline, but in abscess of bone it is sometimes acid.

The *yellow colour of pus* is ascribed to the fatty degeneration of the leucocytes and other cells found in it, and also to the altered blood-pigment and the pigment produced by organisms, e g. *Staphylococcus pyogenes aureus* Sometimes pus is blue, the colour being due to the presence of *B. pyocyaneus*. Pus from the liver is often coloured by bile pigment, and may be chocolate or brownish.

The *odour of pus* varies. Sometimes it may be most offensive, as in some abscesses which develop close to the intestines. The

B. coli communis is often wrongly blamed for this offensive odour; pus due to this organism in pure culture is frequently inoffensive. The offensive odour of pus is often due to an infection mixed with a micro-organism of putrefaction. When connected with the urinary tract, pus is often ammoniacal.

Gas in an abscess may be present either as a product of the invading micro-organism, or as a result of a communication between it and the respiratory or alimentary tract.

These variations in the character of pus are supposed by some to be of value in diagnosis and prognosis; but no great significance can be attached to them. For instance, pus may be identical in appearance, whether it be induced by staphylococci or *B. mallei* (glanders) or *B. pestis* (plague). Therefore the most valuable indications can be afforded only by establishing which micro-organism is the cause of the condition.

Metabolic products.—Apart from the true toxins, pus also contains poisonous products due to micro-organismal metabolism and to leucolysis and cytolysis.

The solid elements.—Flakes of coagulated material and dead tissues may be suspended in the fluid; these may necessitate larger openings for their removal by operative procedure.

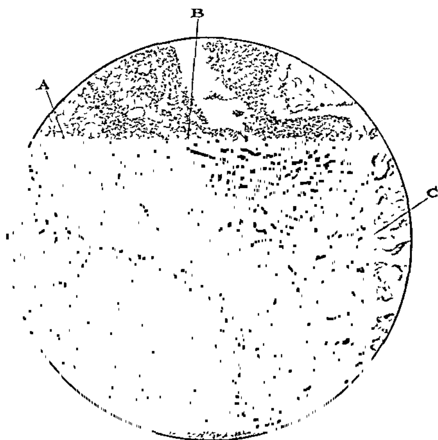
The solid elements consist of bacteria and cells. The most numerous and most representative cells seen in the pus of acute circumscribed and diffuse suppurations are the polynuclear neutrophile leucocytes, and at the present time they are regarded as the most important, and, with the endothelial cells, are the most active phagocytes. *Other leucocytes* appear in pus, notably the lymphocytes, which increase in number with the age of the lesion. The coarsely granular eosinophile polynuclear leucocyte, the hyaline mononuclear leucocyte, the coarsely granular basophile mast-cell (Ehrlich), can all be demonstrated in varying numbers, but they never reach numerical importance.

Endothelial cells, young connective fibrous-tissue cells, plasma cells, and cells of doubtful origin are also seen in pus.

Red blood-corpuscles are seen, and if they are present in large number before the abscess is opened they indicate great intensity of the disease.

The older the abscess, the greater the number of lymphocytes and connective-tissue cells that appear at the margin.

The proliferation of polynuclear neutrophile leucocytes in the bone-marrow and spleen is increased in suppurative processes. The small mononuclear cells (lymphocytes) are not greatly increased in the blood, even in the more chronic forms of suppuration, in which they are present locally in large numbers; therefore they are probably of local origin, and are probably derived from endothelial cells.



Subcutaneous tissue of guinea-pig, seven days after infection with staphylococci. A, Adipose tissue; B, hypertrophied band of fibrous tissue containing highly organized new blood-vessels; C, abscess cavity. × 50.

PLATE 26.

To investigate all the unsettled problems which surround the method by which leucocytes collect in the area of suppuration would be beyond the scope of this article. It is known, however, that the leucocytes escape from the smaller veins and capillaries, but the mechanism of the process is still a matter of speculation. The faculty of amœboid movement which leucocytes are known to possess is a tempting explanation of their mode of progress from the blood-vessel to the seat of disease. The facts that light, heat, galvanism, gravity, chemicals, atmospheric pressure, and so forth are capable of attracting or repelling leucocytes, many plants and lower organisms, have been demonstrated; one or more of these attracting influences would readily supply the force which calls the amœboid power of leucocytes into action, causing them to progress in a certain direction, viz. towards the seat of disease. Other observers maintain that even the amœboid action of the leucocyte may be explained by differences in surface tension, first between it and the inner vessel wall, and then between it and the tissues with which it subsequently comes in contact: and that besides this difference in surface tension the progress of the leucocyte towards the abscess is aided by the direction of flow taken by the fluid exudate.

The *fluid element* of pus is yellow or yellowish green and transparent. It does not coagulate spontaneously, but does so on the addition of nitric acid. Many of the substances held in solution are products of the micro-organism. Besides the toxins, to which allusion has just been made, there are other bacterial substances, such as cytolysin, leucolysin, and hæmolysin.

The substances produced in the tissues by staphylococci, *Streptococcus pyogenes*, and *B. pyocyaneus* possess the property of destroying leucocytes (leucolysin). Leucocytes treated with this substance are identical in appearance with those seen in pus. Denys and Van der Velde separated from the pleural exudate of rabbits inoculated with staphylococcus a substance they termed "leucocidine"; it is highly poisonous and kills leucocytes in a few seconds. The exudate loses this property upon being heated for ten minutes at a temperature of 60° C. These authors have obtained an antibody, which they term "anti-leucocidine," and which is found to be capable of neutralizing the action of leucocidine.

The fluid element of pus also contains autolytic substances derived from the destroyed cells of the host.

Like blood-plasma, from which it mainly comes, the fluid element of pus contains no fibrinogen. It is richer in the proteins, serum albumin and serum globulin, than is ordinary lymph. The fluid of pus also contains albumoses and peptones derived from the killed leucocytes and other tissue cells. Lecithin is more abundant than

in blood. Leucin and tyrosin have been found. Sodium chloride is present, also carbonate and phosphate, to which the alkalinity of pus is due.

Sir Almroth Wright has demonstrated the presence of substances which he calls opsonins in the serum of blood drawn from patients suffering from infective processes, but no opsonin is demonstrable in pus. After an abscess has been opened, however, opsonins appear and gradually increase in amount in the serous discharge.

I have killed rabbits suffering from mature circumscribed abscesses by injecting the animals, some with carmine, others with methylene blue; in none could I observe any pigment within the abscess cavities, though it remained fixed in all the other tissues of the body, including those immediately surrounding the abscesses. This was true also in animals killed by the same process in which the abscesses were opened previous to the injection of pigment. These experiments appear to indicate that there is no direct open lymphatic communication between the body and the abscess cavity; also that the cells of the capillaries and small veins play some part in deciding what shall pass into the abscess cavity. Vice versa, the periodic rise of temperature at night in many cases of toxæmia does not support the theory that mechanical pressure induces absorption from the abscess cavity.

The proteolytic enzymes derived from the leucocytes of pus are probably a cause of death of the cocci, which are killed without being incorporated within cells.

2. When the proliferation of pre-existing tissues occurs around the site of an acute circumscribed abscess, the reader should regard the lesion as being an acute diffuse suppuration the spread of which has ceased. He must not be misled into the idea that its apparent enclosure by connective tissue has led in any way to the arrest of spread; it becomes circumscribed because the process has been arrested. In other words, the proliferation of the connective tissue and the apparent encystment of the abscess cavity cannot be regarded as the cause of its arrest. Proliferation of the local connective tissue could not occur had not the tissues gained a power of resistance which they did not possess during the first hours of invasion The reader will remember that death of tissues was the first consequence of micro-organismal invasion; proliferation of tissue and death of tissue could not exist in association, at the same spot, and under the same conditions The dead parts must have been more susceptible to disease than the proliferating parts.

The state of affairs seen is as follows: At an early stage there is practically no change visible in the activity of the undestroyed cells of the part. The number of leucocytes is increased at the end of twenty-four hours, and in parts they have reached the pre-existing

bands of fibrous connective tissue, but it is the mere accident of collision It may be said at once that, although the endothelial cells increase, and play an important part in phagocytosis, the main and most obvious proliferation occurs in the supporting connective tissue. In forty-eight hours the proliferation of local connective-tissue cells has begun, and young blood-vessels can be seen forming in the multiplying tissues. This proliferation continues, and even when the abscess has reached its greatest maturity and shows no further tendency to spread, it is not completely surrounded by fibrous tissue There may be many points where the pus cells and micro-organisms lie apparently in immediate juxtaposition to the adipose or fibrous tissues Thus the local condition is recovering in the absence of mechanical limitation, and therefore, as stated above, recovery and localization of the process cannot be due to a mechanical circumscription which does not exist. In further consideration of this point it will be remembered that I have already drawn attention to the remarkable microscopical appearances at the margin of an abscess that had been in existence only 48 hours I took particular care to point out that this margin consisted of a sinuous line of heaped-up micro-organisms among recently proliferated unconnected connective-tissue cells Their appearance seems to me to show that even at this early stage the micro-organisms have lost great power in attack and the host has gained great power in defence, but there is no encysting wall in existence at this early stage

The older writers attached too great importance to the circumscription of an abscess by means of the newly formed fibrous tissue; believing it to be the predominating effort of nature to effect the final cure of the malady, they neglected the whole question of local and general actively acquired immunity In considering the value of an abscess wall and the attitude to it which the surgeon should adopt in treatment, the reader must bear in mind that there are other and more fundamental curative forces at work than the incomplete enclosure of an abscess by fibrous tissue, forces which are specific against the particular micro-organism that has caused the disease. The attitude of a surgeon towards the margins of an abscess should be the same whether the lesion be old enough to be more or less encysted or not. At any age of an abscess its margin should be treated with very great care and tenderness The importance of leaving undisturbed every part of an abscess wall is greater in some infections than in others In the treatment of an abscess due to staphylococcus it is wiser always to deal very tenderly with the living margin of an abscess, not mainly because its mechanical disturbance may disseminate bacteria, but rather because mechanical injury lowers the local immunity and provides a more acceptable nidus for the bacteria.

When pus has collected it should be carefully removed before attempting any rough manipulations which it may be necessary to inflict on the margin of the abscess in order to remove an appendix, for instance, or a Fallopian tube. The pus having been removed, it is quite safe, in most cases which are not of a tuberculous nature, to manipulate parts as freely as necessary; in fact, it is wiser to remove the main sources of infection than to leave them for fear of destroying the integrity of the encysting tissues, always provided that first the pus has been removed. Death rapidly follows the rupture of a large tubal abscess into the peritoneal cavity; the early fatal issue cannot be due to the liberation of bacteria into new fields of operation, but is due to the pouring of a highly poisonous fluid from a cavity whose power of absorption is small into a cavity whose power of absorption is great.

Supposing the infection results in an acute diffuse suppuration instead of one which is acute and circumscribed, then those parts where the disease has lasted longest without spreading resemble the margin of an acute circumscribed abscess of the same age; in other parts of the circumference where it is spreading the appearance resembles that of an acute circumscribed abscess of about twenty-four or forty-eight hours' duration

3. As the abscess approaches the skin and before it actually reaches it, the hair-follicles, sebaceous glands, sweat-glands, and superjacent epithelium undergo atrophy and disappear. The last thing seen before the abscess ruptures is burrowing of the pus beneath the horny layer of the skin, which finally gives way, and then the abscess "bursts."

An abscess assumes a round or oval shape partly from the marginal spread from a central point, partly from the centrifugal pressure which it exerts upon the surrounding unaffected tissues, and partly from the centripetal force of the elastic surrounding tissues.

There is difficulty in accounting for the fortunate tendency of an abscess to spread towards the skin. Some writers say that the spread in the direction of least resistance accounts for abscesses spontaneously opening into bronchi, intestines, bladder, pleura, and veins, causing those complications which would naturally follow such accidents. Action of muscles and pulsation of arteries are assumed to be capable of forcing an abscess towards the external surface by *vis a tergo.*

Natural and easy pathways no doubt aid extension to the skin. In many sections of acute suppuration in skin I have seen the advancing process spreading in oblique lines towards the surface, these lines corresponding to the site of the lymphatic vessels which accompany the arteries supplying the skin The microscopical appearances do not suggest that the invading process is being pushed into parts unwilling to receive it; and I am inclined to believe that local

susceptibility is a great factor in influencing the direction of the spread of the disease.

Symptoms.—These are due to the absorption of toxic products, some of which are the toxins produced by the micro-organism, while others are derived from the poisonous products (autolysins) of the body cells

Local.—The first indication of trouble is a sensation of tension in the part, gradually increasing to a definite throbbing pain, which is exaggerated when the part is dependent and diminished when it is raised or placed in warm lotion Lowering the part increases venous congestion; raising it diminishes the congestion by causing a reflex *contraction of arterioles*, as Lister pointed out, and by gravitation emptying the veins. Lister also showed that lowering a limb causes a reflex vaso-dilatation. There is an extreme degree of tenderness, which upon the *slightest touch becomes exquisite pain.* The part is hot, bright red, swollen and hard; its function is arrested. The redness disappears on pressure, but reappears instantly as the pressure is removed As the lesion matures, this reaction becomes sluggish; from being red the centre becomes blue, and soft to touch; this is the first trustworthy sign that suppuration has begun. The part becomes œdematous, and the swelling grows more prominent and tense until fluctuation confirms the fluid nature of its contents. The skin covering the surface becomes thin, shining and polished by the subjacent pressure of the increasing abscess. Around the tense, painful, and red swelling there is œdema, which gradually disappears in the parts farther away from the swelling. The central thinning increases till the skin becomes a translucent membrane, through which the white or yellowish pus can be seen presenting the familiar spectacle of a "pointing" abscess. The skin at this stage may not be quite so tense, for the ulceration of its deeper layers has relieved the greatest tension The diminution of tension is indicated by a very fine network of lines or wrinkles which can be seen in the epithelial surface covering the most prominent part of the abscess. The abscess is quite mature now, and upon the slightest movement or trauma will burst.

The redness disappears immediately upon the rupture of the abscess The part, which up to this time has been held rigidly still by unconscious muscular effort, is now relaxed. At first the pus flows freely owing to the internal pressure in the abscess and the external pressure exerted by the elastic tissues around, which are no longer stretched; contraction of muscles in the immediate neighbourhood also aids the expulsion The pain and swelling gradually subside, and function is restored The abscess walls gradually fall together from want of support and from the continued contraction in the tissues around them.

The gross clinical signs cease to be apparent, although the tissues which formed the margin of the abscess still contain multitudes of micro-organisms; the time of the complete disappearance of the micro-organisms varies in different cases from days to years.

The lymphatic vessels which drain the affected part may or may not be seen as branching, more or less straight, red lines, stretching from the area of disease towards the nearest lymphatic glands; they are *most evident in streptococcic and acute staphylococcic lesions.* The nearest lymphatic glands are frequently enlarged and tender, and give rise to a sensation of local stiffness. The lymphatic vessels may, however, pass the nearest glands without obviously affecting them, and empty into more distant glands. The enlarged glands may become adherent to each other, and confluent if they suppurate. If suppuration has not occurred, the adherent glands may, upon subsidence of the local disease, *gradually become discrete* and, after a time, possibly as long as a year or two, may become practically normal in size. Suppuration may appear in any part of the lymphatic vascular tract between the local disease and the lymphatic glands. In lymphangitis of this kind, I have observed that bursæ intervening *between a lesion and the lymphatic glands into which it drains suppurate* as if they were in direct lymphatic communication. The bursa patellæ, the bursa over the olecranon process, and the bursa under the gluteus maximus, I have seen as the only foci in secondary suppuration of this kind. In the olecranon bursa there was no suppuration at the primary seat of infection.

Constitutional.—The poisoning, which may be profound, is attended by rapidly increasing weakness, loss of weight, dry tongue, night sweats, and vomiting. The patient looks and feels ill, and may fall into the typhoid state; his anxious expression and occasional mental depression are marked and diagnostic features of the condition.

PYREXIA.—One of the commonest and earliest constitutional indications of impending suppuration is a rise of temperature following a rigor, or sensation of chilliness, or an inclination to shiver. Most suppurative conditions are accompanied by fever, but the absence of fever does not indicate a mild infective process. Many cases of severe and even fatal illness may never exhibit fever higher than 99° or 100° F. The height of the fever may vary in different individuals, although it may be caused by the same micro-organism. Fever affords no clue to the identity of the micro-organism. It is due to the products of micro-organisms, to metabolic substances, and possibly also to autolysins, which are thrown into the circulation from the blood- and tissue-cells killed during suppuration.

The varieties of pyrexia in suppurative processes are (1) sapræmia, (2) septicæmia, and (3) pyæmia.

1. *Sapræmia*, of which there are two forms, is due to the absorption from the wound of the products of micro-organisms. The micro-organism remains fixed in the diseased part, and its escape into the circulation is not a marked feature.

One form of sapræmia is *traumatic* or *surgical fever*, in which the products of the micro-organisms are capable of acting adversely upon the living and dead tissues and upon the fluids of the part (parasites). It is the type of fever most commonly seen in ordinary practice; in former days it was the usual result of operative procedures—hence its name There may be an initial fall of temperature to about 97° F., though usually the temperature rises at once to its maximum height of about 103° F At that point it may remain for a day or so, then it gradually falls at the rate of a degree daily until the normal level is reached, at which it remains, the pyrexia having lasted three or four days. Traumatic fever is often the precursor of subsequent more severe types of pyrexia

The other form of sapræmia has little to do with suppurative processes. It is called *septic intoxication*, and is due to the absorption of products from those micro-organisms which are capable of attacking dead tissues only (saprophytes). The temperature rises to about 103° F, and there remains until the infected and dead tissues are removed, whereupon it becomes normal.

2. *Acute septicæmia or bacteriæmia* —The micro-organisms are not only in the site of suppuration, but they have escaped into the blood and tissues of the body, and are there active. Hence this is a more serious condition than traumatic fever. There are no secondary foci of suppuration, and, although acute septicæmia accompanies some suppurative processes, a primary focus of suppuration is not essential. Acute septicæmia may kill an animal in seven hours after injection with streptococcus, and show no signs of suppuration at the site of inoculation or anywhere else Acute septicæmia in animals is more typical than in man. The blood and some viscera (liver, lungs, spleen) may be found teeming with bacteria in animals which have died in a state of acute septicæmia, but in man this is not a very salient feature. The heart-blood and viscera may or may not be able to provide material even for a culture of the micro-organism The number of micro-organisms in the blood and tissues of man bears little or no comparison to their universal and overwhelming presence in animals.

The condition of acute septicæmia may begin and end characteristically, or it may follow traumatic fever immediately or after an interval of a few days during which the temperature may have been normal. When acute septicæmia is established, the temperature rises to about 104° F., it may remit a degree or so during the day, but it rises again at night, and never falls to or below normal until

recovery occurs. The temperature, therefore, is of a remittent, not of an intermittent character. Its decline is usually gradual (lysis), or it may be abrupt (crisis). If death should supervene, a patient may die in a state of hyperpyrexia, and the temperature, it is said, may rise a degree or so immediately after death. In very profound toxæmia the temperature may be subnormal, especially before death. Rigors rarely occur.

The disease may be caused by many organisms, but is usually associated with streptococci. The lesion through which the virus has gained entrance is frequently small, and may escape notice altogether; it may follow a scratch inflicted during the handling of infected dead animal tissues, or occasionally even during operations, or it may follow cellulitis, erysipelas, or gangrene.

Clinically, the patient shows symptoms of acute toxæmia and high fever. He is usually flushed, though in the severest forms and later stages he is often very pale, and may be tinged with yellow. He suffers from headache, malaise, anorexia, albuminuria, and usually diarrhœa. Blood may be found in the urine and perhaps in the stools, and there may be a petechial rash. The nerve-centres are poisoned; the patient becomes delirious, dyspnœic, comatose, and dies.

The prognosis of acute septicæmia, when once definitely established, is extremely unfavourable. A very large proportion of the patients die.

Hectic fever, or chronic septicæmia.—This form of fever also may be introduced by an initial traumatic fever, but instead of the temperature remaining elevated it rises about six o'clock in the evening to between 101° and 102° F, and in the morning it is normal, or even subnormal It is associated with chronic suppurative processes. It is accompanied by night sweats and dryness of the tongue, and lardaceous disease is often a pronounced feature when hectic fever has lasted for some months.

Hectic fever is due to the action of micro-organisms which remain mostly in the diseased part; they can be detected in the blood only with the utmost difficulty.

3. *Pyæmia*, like septicæmia, with which it may be associated, is a dangerous disease, it is probably the more dangerous of the two. It may be caused by any of the pyogenetic organisms, perhaps most commonly by staphylococci. Pyæmia is always associated with an infective thrombosis of the veins at the seat of infection, and is especially liable to follow septic invasion of venous sinuses in the cranium or the puerperal uterus, or of bones. The emboli which separate from a disintegrated thrombus are the causes of the secondary abscesses which form, chiefly in the lungs, and which are

a distinctive feature of this disease. Occasionally it is associated with malignant endocarditis, as the result of detachment of infective emboli, and their infection of the cardiac valves.

Clinically, the fever may or may not be initiated by traumatic fever, and the normal temperature may even have been reached and maintained for about eight days, when suddenly the patient suffers from a rigor, which may be prolonged for about half an hour The rigor is followed by a rise of temperature, to 104° F., which falls in an hour or so to normal, or even below normal; the fall of temperature is accompanied by profuse perspiration and sensation of warmth, after which the patient will feel well and comfortable In severe cases the patient soon experiences another rigor, this may be repeated many times in twenty-four hours; or, in milder cases, the rigors recur at longer intervals, say, once a week or a fortnight. The tongue is dry, and red or brown, and the breath has a curious sweet odour that has been compared to that of hay. The skin is hot, of a dull, pale colour, and may show rashes of an erythematous or petechial character, or sometimes tender hyperæmic areas that are probably the manifestation of lodgment of emboli that have not progressed to definite abscess-formation. The rigors are followed in from three to five days by the appearance of secondary abscesses, which sometimes are characterized by a rapid, insidious, and comparatively painless development. In the typical acute cases, patients usually die in about fourteen days, having suffered constantly from severe rigors The condition is associated with hæmorrhagic infarcts in the lungs, which soon become purulent; but other parts, such as pleuræ, joints, brain, liver, spleen, kidneys, heart muscle, pericardium, and endocardium, may be affected later In pyæmia arising from a focus in the portal system, the liver is the primary site of lodgment of the emboli.

Chronic pyæmia is a condition in which there are no infective thrombi and no embolic foci of suppuration which are typical of true pyæmia; but a secondary collection of pus may occur in any part of the body, notably in the subcutaneous and intermuscular tissues and joints, and is probably due to those micro-organisms which are occasionally carried about by the blood during infective processes finding a suitable nidus. The fever and toxic symptoms are of a milder character and the prognosis is more favourable than in true pyæmia, provided the abscesses are in accessible positions, and the general strength of the patient is well maintained. The temperature of patients suffering from chronic pyæmia may be exceedingly variable

Degenerations.—Suppuration may give rise to cloudy swelling and to fatty, hyaline, and amyloid degenerations

Amyloid disease occurs chiefly in prolonged suppuration, and practically always affects several organs—first either the spleen or the liver, then the kidney, less often the small intestine, and other organs or tissues

The homogeneous newly-formed material is deposited in the cardio-vascular system, and as the disease advances the functional cells atrophy from pressure, and probably also from a diminution of the blood-supply

The affected organ is enlarged, firm and pale, with a semitranslucent, waxy appearance. In the case of the spleen the Malpighian bodies may be affected chiefly, giving rise to the condition called "sago spleen," or the walls of the vascular sinuses in the pulp may show the more advanced change. In the capillaries the disease is outside the endothelial lining which may show fatty degeneration. In larger arteries the deposition and infiltration occur in the delicate fibrous tissue of the middle (muscular) coat In advanced amyloid disease the connective tissue in other situations may also be affected.

The blood in suppuration.—The blood-pressure may be subject to slight variations T G Brodie and I demonstrated a considerable fall of pressure on injecting into the veins large doses of a culture of staphylococcus

In suppuration many changes are induced in the blood and tissues in connexion with (1) the cell element, (2) the plasma element.

1. The cell element. i *Leucocytosis*—In suppuration not due to actinomyces or *B. tuberculosis* or *B typhosus*, leucocytosis is marked unless the disease be rapidly fatal or of a profoundly toxic type, in which case it is absent, or the leucocytes are diminished in number (leucopenia). In a common type, leucocytosis increases with the development of the disease; it subsides shortly after the disease has disappeared, when the number of leucocytes may be fewer than normal The presence of pronounced leucocytosis is a valuable sign; by some it is considered sufficient to justify a good prognosis In those cases which ought to show a leucocytosis, but which actually show a leucopenia, the prognosis is decidedly bad. The presence of leucocytosis is a valuable indication in the diagnosis where suppuration is occurring in obscure parts

ii *Phagocytosis.*—In suppurative changes the products of micro-organisms give off substances which induce an active migration and proliferation of leucocytes. All leucocytes possess the power of ingesting micro-organisms, but the lymphocytes and eosinophile leucocytes do not possess it to a great degree. Although the polynuclear neutrophile leucocytes are the most active phagocytes, they exhibit much variation in the number of micro-organisms individual cells take up. Besides the leucocytes, endothelial cells are phagocytic, perhaps more

so than any other tissue cell. Giant cells, which are probably derived from endothelium, are also phagocytic In suppurations due to the gonococcus, epithelial cells share in phagocytosis.

Besides the inclusion and digestion of micro-organisms, phagocytes can absorb cells which are foreign to the body, cells killed in the process of suppuration, red blood-corpuscles, foreign bodies (ligatures, etc.), and they are capable of removing small necrotic areas. The reader is referred to the section on Immunity (p. 28), where he will see that protection and recovery from infective diseases, although closely associated with phagocytosis, is not a simple matter of cell incorporation and intracorporeal digestion.

There can be no doubt that in suppurative conditions phagocytosis bears a very important part in the fight for life and eventual recovery of the patient. What that part is, in the light of present knowledge, will be found set out in the article on Inflammation (p. 144). All that need be said here is that phagocytosis is most evident in the cells of pus; that in the liver and spleen the micro-organisms can be seen incorporated in leucocytes quite early in the disease; and that the same process can be seen occurring in the blood-stream—a fact more noticeable in the more severe cases.

iii *Anæmia* is a very constant accompaniment of suppurative processes, and no doubt is in part due to a solution or destruction of the hæmoglobin in the red blood-corpuscles by the hæmolytic substances formed by micro-organisms.

2 **The fluid element.**—In the blood-serum, as in the pus, in cases of suppuration, the specific toxin of the invading micro-organism, the by-products of bacterial metabolism, and other poisonous substances which result from the autolysis of cells killed in the process, are present. Besides these substances the blood-serum may contain antitoxins, opsonins, agglutins, bacteriolysins, precipitins, and aggressins

Diagnosis.—It must not be assumed, because a swelling contains a thick white or yellowish fluid, that it is the result of suppuration, and that the fluid is pus Fluids with these properties are seen in dermoid and sebaceous cysts; and I have seen malignant disease of the breast diagnosed as a purulent condition on the assumption that the thick yellow fluid in the centre of the growth was pus, but on microscopic examination the cells of the fluid were found to be epithelial and leucocytes were absent. Chylous fluid might give rise to error in diagnosis. I have seen the carpo-metacarpal joint of the thumb of a man suffering from gout full of fluid which, on extraction, looked like, and was assumed to be, pus; but under the microscope the solid elements were found to be only acicular crystals of uric acid

The presence of an acute circumscribed abscess can be readily recognized by the signs and symptoms already described. I will

mention a few of the fluctuating swellings from which it should be easily distinguished. Although *hæmatoma* has a fluctuating centre and an œdematous margin, and, if the swelling be a large one, there may be leucocytosis, it differs from abscess in its sudden appearance after injury (which may be slight in hæmophilia), in the absence of pain, heat, redness, pyrexia, constitutional depression, and enlarged lymphatic glands. On the same lines, *distended gall-bladder* and *urinary bladder*, *collections of synovial fluid*, and *serous effusions* can be diagnosed readily from acute circumscribed abscess. Also, *synovial* and *serous effusions of a non-infective nature* allow more functional activity than in the suppurative conditions. The association of an abscess with an *aneurysm* may be difficult to diagnose; many have been opened in error, especially in ulcerative endocarditis, where infected emboli have blocked the lumen and softened the walls of arteries, e.g. at the bifurcation of the brachial artery; but the real state of things can be determined definitely by a careful consideration of the history, by the suspicious anatomical relation to a big artery, and by the additional signs which may be present and which are indicative of a dilated blood-vessel. Dermoid, hydatid, sebaceous, and other *cysts which are undergoing acute suppuration* are often impossible to diagnose from an uncomplicated acute circumscribed abscess; the history, and proper examination of the contents and margins of the lesion, should determine exactly the real nature of the disease.

No surgeon ought to be satisfied to make a diagnosis merely of acute circumscribed abscess or acute diffuse suppuration: that is not an exact diagnosis, for the condition may be caused by many agents, and specific treatment may be indicated by the discovery of the actual micro-organisms of invasion. The prognosis, too, depends upon the knowledge as to which of many micro-organisms the patient is actually fighting. The clinical signs may help the diagnosis, but they cannot be trusted, and should always be controlled by a complete bacteriological examination. For instance, a localized acute abscess, such as a boil or carbuncle, is more frequently due to a staphylococcus than to any other infection, but an analogous condition may be induced by *B. typhosus*. When a localized abscess is complicated by extensive lymphangitis it may be a streptococcus lesion, but as marked a lymphangitis may be the result of a highly virulent staphylococcus. On the other hand, even a virulent streptococcus may be extremely local in its action.

A complete bacteriological examination must take account of (1) the blood, (2) the pus and the abscess wall.

1. In the examination of the blood its opsonic index may be estimated (though of late years the strenuous nature of this investigation has prevented most people from its constant employment),

and the leucocytes examined qualitatively and quantitatively, and especially cultures should be made from it. The amount of blood withdrawn for examination should be from 5 to 10 c.c. Care should be taken to determine the agglutinating property of the serum towards the suspected micro-organism; this is especially valuable in case of *B. typhosus* (Widal's reaction), *B pyocyaneus*, and *B. coli*. In staphylomycosis and streptomycosis I have not been able to satisfy myself that the application of homologous serums aids the diagnosis

2 In most cases of acute circumscribed and acute diffuse suppuration, examination of the pus alone will afford all the evidence needed, but a more certain method of demonstrating the micro-organism is to examine a scraping from the margin of the abscess cavity. The examination, to be complete, should include staining, growth on artificial media, plate cultivation, and inoculation into animals It should be conducted in all cases in which the least doubt exists, and in those patients in whom recovery does not occur as rapidly as the surgeon would expect, and where, possibly, a more serious infection exists than that which he believed he was treating. But to examine the blood, and stain, cultivate, and inoculate the tissues into animals, in every case of suppuration, is not possible in ordinary practice. The minimum practice should be to stain pus or a scraping from the margin of the disease in all cases of suppuration; should the clinical behaviour of the case correspond to the usual results caused by the micro-organism discovered, nothing more need be done unless a vaccine for its treatment be desirable: in this case a culture, and probably a plate culture, must be made

Treatment.—The treatment both of acute circumscribed abscess and of acute diffuse suppuration must be (1) local, and (2) constitutional

1. **Local.** i Preventive.—It has been suggested that as a part of the preparation of cases for operation, where the wound is likely to suppurate on account of its proximity to septic sources, a preliminary injection of antitoxic serum or vaccine should be given. Unfortunately it is not as yet possible to obtain an antitoxic serum that protects an animal with any degree of certainty from the toxins produced by any of the micro-organisms which induce suppuration. Antistreptococcic serum, in my experience, is practically valueless The same may be said of a serum which W. Bulloch and I obtained from a horse that we inoculated with staphylococcus; the serum obtained was quite ineffectual either as a preventive or as a curative agent.

A more hopeful preventive of suppuration than any antitoxic serum is the preliminary inoculation of vaccines, and perhaps in cases where extensive and dangerous suppuration is expected it would be

wise to inject the vaccines of staphylococcus and streptococcus before operation. It must be remembered that there is a negative phase after the injection of each vaccine; during this the patient is more susceptible to the effects of those micro-organisms against which protection has been attempted. Among the practical *difficulties* which arise in connexion with this matter is the fact that there are so many micro-organisms against which a surgeon would like to protect his patient before operation. Each vaccine will protect the patient against its own micro-organism only, each has a negative phase, and in many cases the artificial immunity induced is of very short duration. However, it would be the duty of every surgeon to disregard these difficulties, and adopt the procedure in all cases if there were strong practical reasons for doing so. But, as a matter of fact, the observance of correct antiseptic principles and methods is able to overcome all the septic complications which are likely to arise in ordinary practice. I have adopted the preliminary preparation by vaccine treatment in tongue, mouth, and rectal operations; the vaccines of the staphylococcus, streptococcus, and colon bacillus were administered; but I cannot say that the cases did better than those in which only antiseptic measures were used. There can be no doubt that in some diseases it would be well to prepare the patient by the administration of vaccines, in the hope of diminishing the risk of the evil effects which might result from dissemination of micro-organisms; for instance, of *B. mallei.*

ii. Palliative.—The importance of *rest* cannot be exaggerated in all stages of infective processes. This can be effected by the aid of splints, etc.

Hot fomentations.—The parts should be shaved, and the skin of the diseased and neighbouring areas purified. The fomentation cloth should be plain lint; after being wrung out of a boiling solution of perchloride of mercury (1 : 8,000), and laid on the prepared parts, it should be covered with sterilized mackintosh so that the cover overlaps the hot lint for three-quarters of an inch all the way round its edge; this, again, should be covered with wool and gently bandaged; where possible a many-tailed bandage should be used, to save unnecessary manipulation of a very painful part. A warning should be given against the use of carbolic fomentations on fingers and toes, where localized gangrene may readily be caused by the use of this dressing. A limb should be raised and put on a splint in the position in which it is most comfortable; all natural hollows between limb and splint should be carefully padded. In these circumstances, should the abscess burst, the pus will come in contact only with purified parts and dressings. Hot fomentations act also as counter-irritants.

Spongiopilin may be used instead of the fomentation cloth and

mackintosh Antiphlogistin and Unna's 88-plaster are said to possess valuable palliative properties.

It is hardly necessary to state that poultices made with bran, bread, linseed, carrot, onion, charcoal, etc., are not to be employed.

iii. OPERATIVE.—Directly the presence of pus is determined the abscess should be opened. All the steps should be taken which are commonly adopted in ordinary sterilization of the hands of the operator, skin of patient, instruments, etc. The fact that the surgeon is dealing with infection affords no reason for relaxing his endeavours to keep out other infective agents.

The site usually selected for the incision is that part of the abscess where the skin is thinnest, i.e. where the abscess is "pointing." The direction of the incision should be parallel to important vessels, nerves and ducts, to avoid wounding them The length of the incision must be sufficient to admit a small sterilized swab, wrung as dry as possible from a solution of perchloride of mercury (1 : 2,000) or other antiseptic, to break down septa that may separate recesses from the main cavity, and to remove as much of the necrotic tissue as may be detached easily from the inside of the lesion. The question of drainage is discussed below Rest and splinting should be continued, and the parts should be dressed with gauze, or the hot fomentations can be continued if pain is severe

The abscess will usually recover completely and rapidly; but if it does not, antitoxin and vaccine treatments should be adopted as the symptoms and the nature of the micro-organism indicate

In carbuncle there is so much necrotic tissue that an incision is not enough to evacuate the contents; hence complete and wide excision is the best treatment. Some surgeons prefer to incise the carbuncle and scrape away the necrotic tissue with a sharp spoon Some apply pure carbolic acid to the tissues surrounding the inside of the cavity after scraping away the necrotic tissue, but in ordinary staphylococcus lesions this is quite unnecessary. In practice I have had better results from using fuming nitric acid than pure carbolic acid in acute suppurations due to *B. mallei* The nitric acid may induce a greater flow of serum than the carbolic acid, so the better results obtained may be explained by the encouragement of conditions which stimulate local immunity rather than by its destruction of micro-organisms.

Drainage.—The best drainage is obtained by the use of india-rubber tubing, as large as possible, and perforated at intervals. Small holes are essential in abdominal work, as I have seen a coil of intestine fixed irreducibly in a large hole made in a large tube, and causing signs of acute intestinal obstruction. After insertion, the external extremity should be level with the skin surface, and a loop of silk-worm gut should be tied in the tube to act as a guide in case it

disappears within the cavity; for want of this precaution tubes have been lost in the antrum of Highmore, the pleural and peritoneal cavities, and have given rise to prolonged suffering in consequence. Drainage is essential in abscesses which are deeply situated and in bony cavities; but in the ordinary superficial abscess of soft parts drainage, except for a very short period, is unnecessary; in fact, it is contraindicated, because the tube forms a convenient pathway down which contaminating micro-organisms can gain access. To prevent a drainage-tube from becoming a channel for the growth of micro-organisms from the skin, I have adopted the plan of wrapping antiseptic gauze like a collar round the extremity of the tube which is in contact with the skin. After a few hours the tube only drains the cavity which it fills; and, moreover, being lifeless, it possesses no intrinsic power to aid local immunity. In fact, I have constantly observed that so long as a tube is present the micro-organisms which caused the disease can be found on it and in a highly virulent condition, and that the discharge of serum rapidly ceases on removing the tube, which has been acting as a foreign body. Gauze "wicks" do more to dam up a wound than to drain it. If it be feared that the epithelial surfaces in contact with one another may obstruct the outflow of an abscess cavity, an elliptical excision of the opposing surfaces will prevent this, and obviate the necessity for a tube. Abscesses due to *B. tuberculosis*, if they cannot be completely excised, should be opened and afterwards sewn up to prevent the contamination that would almost certainly ensue from the constant presence of a drainage-tube.

Hilton's method of opening an abscess is employed when pus has collected near important structures, e.g. the blood-vessels and nerves of the neck. An incision is made in the skin, then a closed sinus forceps is forced through the intervening tissues into the abscess cavity, and the blades are opened in the direction parallel to the structures which the surgeon desires to avoid.

In the treatment of large ramifying infected wounds the Carrel-Dakin method was very popular during the war. Before its employment the dead tissues are freely removed, and many tubes of small calibre (Carrel's tubes) are carefully inserted into all the recesses and the wound is kept irrigated with Dakin's hypochlorite solution. The irrigation can be maintained by one of two methods. (*a*) The tubes are connected with the suspended vessel containing Dakin's solution by means of a large long tube, by clamping and unclamping which irrigation may be constant or intermittent respectively. (*b*) Each Carrel tube is syringed separately every two hours; this method is more irksome, but it guarantees the efficiency of each tube, and the bed and the patient are not so liable to be swamped.

In the wounds that occur in civil practice the employment of this

method is not so valuable. Its use is limited to deep suppurating abdominal and pelvic cavities where dependent drainage is difficult to provide. It is useful in the deep, long trough of an exposed medullary cavity of bone in the treatment of acute osteomyelitis, of the tibia for example; also in the treatment of septic joints—the knee-joint for example, where again dependent drainage is difficult to secure

Dressing.—The wound should be dressed with antiseptic gauze. For the first few hours sterilized "green protective" should cover the lips of the wound to prevent the gauze from sticking to them, thereby relieving the patient of pain when the dressings are removed. Hot fomentations of gauze wrung out of boiling solution of perchloride of mercury (1 . 8,000) for the first few hours have also a soothing effect on acutely inflamed tissues

2. The **constitutional treatment of an acute circumscribed abscess** depends a great deal upon the clinical course of the case, and upon the etiological micro-organism.

Upon general principles, change of air to an exhilarating place, food in a nutritious and easily digested form, and attention to the excretory functions are essential. Should the case be doing well, nothing more is necessary; but should the disease spread or remain stationary, then the advisability will have to be considered of an immediate change of air and the administration of a vaccine or an antitoxic serum, as may be indicated, in order to help the patient to acquire immunity

In the case of a *staphylococcus* infection, there is no antitoxic serum of particular value, and the use of vaccine would of necessity be the additional treatment. It is advisable to prepare the vaccine from a growth of the actual micro-organism which is the cause of the lesion, but this is not essential. A dose of 10 millions to 500 millions should be given, and very likely it will be necessary to give two or three more doses at intervals of fourteen days.

In a case of *streptococcus* infection, in which extra immunizing power is needed on the part of the patient, polyvalent antistreptococcic serum, in the hands of some surgeons, has been occasionally very successful; but I have seen no benefits derived from its use, although I have given it extensive trials in both pure and mixed streptococcus infections I tried the serum from a horse which had been inoculated with the patient's own micro-organisms, but with no result, good or bad. The vaccine treatment also should be employed. The micro-organism should be cultivated from the seat of the disease, and a dose of from 1 million to 20 millions given about every ten days.

In *pneumococcal* infections the antipneumococcic serum has not proved of much use in local lesions. Vaccines should be employed

in cases which do not progress, and a dose of 5 millions to 100 millions may be given about every ten days in chronic cases.

Against infections due to *gonococcus* the patient is best reinforced by *vaccines*; there is no trustworthy antitoxic serum for this micro-organism, but I have seen benefit result from the administration of vaccines in doses of from about 10 millions to 100 millions in cases of very chronic suppuration from this cause.

In suppurations due to *B. coli* the only specific treatment is the administration of vaccine. The vaccine should be prepared from the patient, and should be given in doses of from 20 millions to 250 millions.

It may be said of all vaccine treatment that, in suppurative conditions at any rate, the surgeon must be prepared to meet with many disappointments, therefore he must not relax constant care in his *antiseptic local treatment.*

For further details of vaccine treatment, *see* p 109 *et seq.*

ACUTE DIFFUSE SUPPURATION

Acute diffuse suppuration varies only in degree from an acute circumscribed abscess, and the essential points in common have been already discussed. It is a more intense process, and shows less tendency to remain localized; even when the area is quite small, there is no attempt on the part of the tissues to proliferate to the extent seen in acute circumscribed abscess. Its failure to remain localized depends upon (*a*) a greater virulence on the part of the micro-organism, (*b*) a diminished power of resistance on the part of the host; or (*c*) a combination of the above.

The result of the process is a large ramifying cavity containing pus, or a small and even microscopic abscess, showing no signs of inducing local changes except death of tissue and emigration of leucocytes. Death of the host may occur while the suppuration is spreading.

Multiple acute diffuse suppurations may be primary, that *is to* say, a result of the dissemination of the micro-organism immediately after inoculation; they may be secondary, resulting from infective emboli (pyæmia); or they may be due to the arrest, in a part of low immunity, of micro-organisms which have gained entrance to the general blood-stream from a focus of suppuration existing elsewhere (chronic pyæmia). The abscesses so caused vary very much in size, from collections of a few leucocytes to cavities containing large quantities of pus.

Clinical appearances. Local.—When an acute diffuse suppuration is superficial, the skin covering it is painful, hot, red, œdematous and swollen, and may be hard and brawny; the margin is diffuse, and branching lines of red and inflamed lymphatic vessels

may be observed stretching from it towards the nearest group of lymphatic glands Lymphangitis indicates a severe infection. The tissues may be so choked with the exudation of serum and leucocytes that occlusion of the blood-vessels may occur and cause gangrene of the skin. When an abscess of this kind occurs in the deeper tissues the skin may be separated from them by so large a collection of pus as to become deprived of its blood supply, and gangrene may result from this cause

The occurrence of suppuration in a hard, brawny skin is marked by a soft spot in its centre, which can be detected by gently examining the surface with the finger. The presence of pus more deeply situated is marked by fluctuation, pain, throbbing, increase in the size of the part, and œdema of the superjacent skin. Crepitation is a more common sign in acute diffuse suppuration than in acute circumscribed abscess, though it is rare in both; it is due to a gas-forming micro-organism, to the decomposition of the tissues affected, or to gas having gained admission to the abscess by the establishment of a communication between it and the respiratory or the digestive tract

The **constitutional** signs are more severe than in acute circumscribed abscess; they may be associated with the types of temperature which indicate septicæmia or pyæmia.

Treatment of acute diffuse suppuration.—The same general principles must be employed as in the treatment of localized abscesses; but incisions must be free and extensive, and two or more incisions must be made where the skin is likely to become gangrenous. Should extensive gangrene occur, skin-grafting will be necessary after the separation of the dead tissues. Where putrefaction exists, large drainage-tubes must be inserted in the most dependent parts.

In spite of these measures, the process may still continue to spread and may necessitate more incisions Hot local antiseptic baths of perchloride of mercury (1:8,000) or sanitas, or large hot antiseptic poultices constantly applied, may be beneficial, and the Carrel-Dakin method also might be useful.

Vigorous constitutional treatment is called for to reinforce the power of resistance which is evidently lacking. Vaccine treatment may be indicated; and in those cases in which the streptococcus is the agent of infection, antistreptococcic serum should be tried as an empirical measure

SUBACUTE ABSCESS

Subacute abscess may be caused by those micro-organisms which are capable of inducing acute suppuration, or by those which, as a rule, give rise to chronic suppurations The nature of the infecting agent should be ascertained at once, and dealt with accordingly.

Some very serious types of suppuration may be described as subacute, notably those due to *B. mallei*, *B. typhosus*, *B. tuberculosis*, and the fungi which are the cause of actinomycosis.

CHRONIC ABSCESS

The term chronic abscess is applied to suppuration slowly provoked in a cavity of its own formation, and of which the excitant may be localized, or may slowly infiltrate the tissues around it.

Etiology.—It is so common to find the *B tuberculosis* in slow suppurating processes that chronic abscess is almost always assumed to be a tuberculous abscess, and this, too, in spite of the fact that tuberculous abscesses are really degenerations of chronic inflammatory tissue rather than a true suppurative process. When true suppuration accompanies tuberculous conditions it is due to a mixed infection. It must be realized that chronic suppuration, especially in bones, may be caused by the staphylococcus, and that slow suppuration can be induced by the actinomyces, *B. typhosus*, and even *B. mallei* (glanders).

The **pathology** *of abscesses not caused by B. tuberculosis* is practically identical with that of a comparatively slow-forming, acute circumscribed abscess.

Pathology of tuberculous degeneration.—Apart from the all-important presence of the *B. tuberculosis*, tuberculous abscesses have characteristic microscopical appearances.

The cells observed in true chronic infective processes are epithelioid cells, lymphocytes, giant cells, spindle cells, plasma cells, and even mast cells in small number. In tuberculosis these cells are arranged characteristically in two ways which depend upon whether *B. tuberculosis attacks the tissues (a) by the formation of tubercles or (b) by infiltration*

(*a*) In *tubercle-formation* the central cell of a tubercle is commonly a giant cell, whose branches can be traced as a fine network among the surrounding cells, which are epithelioid cells arranged in two or more layers. The outer margin of these layers is abrupt, and is in turn surrounded by lymphocytes. The tubercle may be completed by an external membrane composed of spindle cells where the disease is not spreading rapidly. The central cell of a tubercle is not always a giant cell; very often, indeed, the centre is occupied by epithelioid cells. The *B. tuberculosis* is to be sought in and among the epithelioid cells, where it is usually found; it is also commonly seen in the giant cell, should that cell be present.

The centre of a tuberculous abscess is formed of caseated, firm, undifferentiated and unstainable tissue. A few examples of *B. tuberculosis* can be seen now and then in the mass of caseous tissue. At

the margin of the caseous material the outlines of giant cells, epithelioid cells, and lymphocytes can be discerned by shutting off some of the light. Immediately surrounding the caseous centre can be seen confluent tubercles in various stages of caseation. Externally to this zone are the typical discrete tubercles; they are separated from each other by proliferating connective-tissue cells, in which can be seen thickened blood-vessels and capillaries whose endothelium may be undergoing proliferation. The whole lesion just described may be surrounded by a fibrous-tissue capsule which is more or less complete, and which in old cases may be calcareous.

(*b*) When the bacillus of tuberculosis affects a part by *infiltration*, no tubercles can be seen; the whole lesion is composed of a collection of epithelioid cells, among which here and there a giant cell may be detected. The whole may be surrounded by lymphocytes and fibrous tissue; caseation is more and more marked till the centre of the lesion is reached, where it may be complete. The bacillus is to be found mainly in and among the epithelioid cells, and its presence is less and less evident as the centre of the caseous mass is reached. Whether it affect a part by the " formation of tubercles " or by " infiltration," the main clinical characteristics of the disease are the same.

The giant and epithelioid cells are derived by proliferation from the local tissues, and mainly the endothelium. The epithelioid cell is the most characteristic cell of a tuberculous degeneration; in all forms the *B. tuberculosis* should be first sought among these cells.

Diagnosis.—A tuberculous abscess may be distinguished clinically from an *acute abscess* by the absence of acute inflammatory signs, by the comparatively great thickness of its margins, and by the comparatively little constitutional disturbance to which it gives rise, even in the largest abscesses. The temperature may be normal or hectic in type. The swelling fluctuates. When an abscess travels from the spine to the groin the swelling in the groin gives an impulse on coughing. It can be distinguished from a *femoral hernia* by being irreducible; by appearing outside the main blood-vessels; by the discovery of a deformity of the spine, for which search should be made in all suspected cases. On palpation, fluctuation can be detected above and below Poupart's ligaments, and it is not resonant on percussion. *Fatty tumour, dermoid cyst*, and *hygroma of the neck* are sometimes mistaken for tuberculous abscess.

Amyloid disease may be present, but usually only when the *B. tuberculosis* is accompanied by some other micro-organism.

In all tuberculous abscesses the diagnosis should be made, where possible, by the demonstration of the *B. tuberculosis* in the so-called pus, or, with better chance of success, in the abscess wall. When it is impossible to stain the bacillus, guinea-pigs should be inoculated.

There are other methods which should reinforce the diagnosis made by ordinary clinical and bacteriological observation, especially when the diagnosis remains doubtful. The three methods to be taken into consideration are tuberculin reaction, the opsonic index, and estimation of leucocytes in the blood.

Tuberculin may be employed in one of three ways—by subcutaneous injection, by the skin-reaction (von Pirquet), or by the conjunctival reaction (Calmette). The best and safest method is probably subcutaneous injection They all depend mainly upon the local inflammation, accompanied by a general feeling of malaise, which results in cases where tuberculosis is present; in the cases in which there is no tuberculosis there is an absence of local and constitutional disturbance.

The *opsonic index* may be of value in one of four methods of application :—

1 By taking a specimen of the patient's blood and estimating its opsonic index without special preliminary treatment.

2 By taking the opsonic index after massage of the diseased area.

3. By examining the opsonic index after giving an injection of tuberculin.

4. By consideration of the opsonic index in conjunction with an *estimation of the leucocytic contents of the blood* A high or a low opsonic index is an indication of tuberculosis; when either is accompanied by an absence of leucocytosis and a diminution or absence of eosinophile leucocytes, the diagnosis of tuberculosis becomes surer than when either is considered alone. It must be remembered that there is no leucocytosis in infections of *B typhosus.*

Treatment. Local.—If it be possible to excise a tuberculous abscess, that is the best treatment. When a tuberculous abscess is connected with bone, say a rib, the affected portion of the rib should be removed with the abscess If the abscess be accessible but its complete excision impossible, then it will be wise to excise as much of the tuberculous tissue as possible after the pus has been evacuated The advisability of drainage in a case of this kind is open to question. If drainage be not employed, the abscess is liable to re-form; if drainage be employed, the tube will act as a mechanical irritant and also as a pathway for other micro-organisms, and a deplorable mixture of infective processes will complicate what was before a pure infection of *B. tuberculosis.* The best form of treatment is either to sew up the wound entirely, or to leave the incision open, not inserting stitches or drainage-tubes, and simply to dress the wound with the utmost antiseptic care, with a view to secondary suture Should it be considered advisable to scrape a tuberculous abscess wall where excision is impracticable, it would be well first to scrape with a sharp spoon, and then to apply

pure carbolic acid or iodine to the raw surface with the intention of preventing further local and general infection.

When a tuberculous abscess is large, as in psoas abscess, it is safer to open it and to wash it out with a hot solution of perchloride of mercury (1 : 10,000) to remove dead tissue, and then to sew up the incision. Tuberculous pus may or may not reaccumulate in these circumstances; directly reaccumulation does occur, the operation should be repeated as often as necessary; by this means the cavity of the tuberculous abscess becomes smaller each time, and eventually may be cured permanently A sinus may form and remain discharging a slight amount of sero-purulent fluid for months or years, and will cease only when the spinal trouble has healed. Acting upon these principles, I have treated many tuberculous psoas abscesses associated with disease of the spinal column In some cases no reaccumulation occurs; in others reaccumulation takes place, but the wound afterwards remains healed. Occasionally sinuses result which remain discharging Treatment either by this method or by aspiration should entirely replace the older and dangerous plan of opening the abscess scraping with a sharp spoon, washing out, and draining.

All the modes of treatment should be combined with rest, splints, spinal carriage, sunlight and fresh air etc A more considerable degree of rest should be given to tuberculous lymphatic glands than is the usual practice, they do best when the parts affected are placed in a state of physiological rest

Constitutional treatment should consist of all the well-known means of building up the patient's strength. sunlight, fresh air, the administration of cod-liver oil, iodide of iron, the extract pressed from raw meat, absence of fatigue, and prevention of collateral infective processes such as colds, whooping-cough, measles, decayed teeth, tonsillitis, adenoids, etc

Vaccine and serum treatment.—It may be said at once that there is no serum yet obtained which has value in the treatment or prevention of tuberculosis The only question at present is whether vaccine treatment is of supreme, or of little or no value It cannot be asserted that the evidence in favour of vaccine treatment is convincing. In the majority of cases it is as disappointing to the patient as it is to the surgeon The great lesson to be enforced, so far as this treatment has gone, is that the surgeon must not omit to employ any of the many valuable aids he possessed before it became the vogue. Should the treatment be used at all, its greatest advocates admit that it must be associated with sound and careful surgical procedures, and that on no consideration should the surgeon relax a single detail in the antiseptic precautions.

ANGINA LUDOVICI

This term is applied to a diffuse infective inflammation of the median and lateral aspects of the neck. It may be induced by one of many kinds of micro-organism, but it is caused most frequently by the *Streptococcus pyogenes*, staphylococcus, or pneumococcus. But *B. mallei* (glanders), a bacillus resembling, if not identical with, the *B. diphtheriæ*, and actinomycotic organisms have been found in pure culture in the discharges The primary sources of infection should be looked for in the mouth, tonsil, pharynx, nose, ear, and scalp. The disease is a cellulitis, not a lymphadenitis

It usually starts as a hard, brawny, dusky-red, swollen area of skin about the chin or angle of the jaw. If severe it spreads downwards with a diffuse margin. Pain is not generally a very prominent feature; the neck usually feels stiff and uncomfortable; but in some cases there is great pain, and gradually increasing dysphagia and dyspnœa. As a rule, the disease is more subacute than acute; the fever is slight, but increases with the intensity of the disease. Usually the lesion does not suppurate; but either suppuration may occur in one soft patch in its centre, or the whole area may be the site of a large diffuse suppuration.

Treatment calls for no special remark Local fomentations may be considered, with vaccine- and serum-therapy as the case demands. Incisions have little, if any, effect in shortening the course of the disease where no suppuration is present, but where *suppuration* occurs they must be made freely.

The type of hard, diffuse, brawny, swollen, œdematous, tender and painful inflammation, of which angina Ludovici is an example, is also met with in other parts

ULCERATION

By C. A. PANNETT, M.D., F.R.C.S.

Definition.—A process of gradual disintegration of the surface of skin or mucous membrane and the subjacent tissues; the resulting breach of surface is an ulcer

Ulcers may be divided into the following groups:—

1. Simple, including those of neurogenetic and thermal origin.
2. External ulcers due to specific micro-organisms, e g. syphilitic, chancroidal, tuberculous, actinomycotic, and those of anthrax, tropical ulcer, veldt sore, etc.
3. Internal ulcers of special pathology, e.g. gastric, duodenal, typhoid, dysenteric, etc.
4. Neoplastic

Only the *simple* varieties will be discussed in this article; the others are considered elsewhere.

Etiology.—In the production of a simple ulcer three factors come into play—

1. The application of an irritant, or trauma, which may be mechanical, chemical, thermal or microbic.
2. Lowered tissue vitality, whether due to circulatory or to nervous causes.
3. More or less septic infection.

These factors present themselves in very different proportions; thus severe or prolonged application of an irritant, or trauma, may produce ulceration even in healthy tissues, and, conversely, an apparently negligible injury may lead to it in a tissue of lowered vitality. Pressure will cause local sloughs, partly by causing anæmia and partly by its prolonged traumatic effect. The second factor, lack of vitality, may be due to vascular causes, leading in some cases to local anæmia, in others to local congestive conditions; thus ulceration may follow diminution of blood supply due to surrounding sclerosis or other causes, or, on the other hand, it may be associated with congestion and stasis, as in varicose veins; similarly, ulceration may result from interference with lymphatic return

Circulatory ulcers, those in which the circulatory factor predominates, are therefore common on the limbs, especially below the knee

The actual determining cause is either an injury or an invasion by *micro-organisms, which* can establish themselves the *more easily in* the poorly nourished tissues.

The *neurogenetic ulcer is associated with* some peripheral nerve lesion. The site of the ulcer is usually anæsthetic, so that the *patient* is unaware of the *injury that leads to the breach of surface; in addition*, the circulation may be poor as the result of the nerve disease, and possibly also there is an *associated loss of trophic tone. Examples* of ulcers in which the nervous element predominates are to be seen in ulnar paralysis, in syringo-myelia, *in tabes*, and in anæsthetic leprosy.

Thermal ulcers may be due *not only to burns and scalds* but *also* to the effects of electric currents

Pathology.—A simple ulcer passes *through three stages in its* life-history:

i. The stage of active ulceration or *progressive spread.*

ii. The transitional stationary stage, or that of balance or cleaning

iii The *stage* of healing and repair

The first and third stages run through definite clinical courses, *the second stage* may be quite short and *transitory between the other* two, or it may be prolonged and complicated by certain accidental *circumstances, viz, those of "chronic ulcer" and its sub-varieties* "callous ulcer," "eczematous ulcer," "varicose ulcer," "irritable ulcer," etc.

During the first stage, that of active spread, inflammation and tissue necrosis are occurring In nearly all cases an ulcer, once formed, spreads as the result of infection with organisms from without. The toxins of the bacteria cause death of the cells, which are digested and removed by the activity of the leucocytes. Organisms are found not only on the surface of the ulcer, but also in the subjacent parts Active destructive inflammation exists in the parts immediately surrounding and underlying the ulcer.

During the second stage, active spread has ceased *but true healing* has not yet been established; the ulcer is, however, becoming cleaner, *necrotic tissue is being removed, and preparation* for healing is taking place. Normally this stage should be short. But sometimes it is indefinitely prolonged; the processes of repair are inhibited; the ulcer is then said to be "callous" or "weak."

During the healing stage the surface of the ulcer becomes studded all over with small red protuberant granulations The edges of the ulcer now shelve gradually from the skin level to the floor of the ulcer. There is an outer white margin with an inner blue zone which is formed by a thin layer of new epithelium spreading over the surface. The

discharge now is thick yellow pus, the "laudable pus" of the olde surgeons; the bright surrounding hyperæmia has given place to milder congestion or to the normal appearance.

Pathologically, in this stage leucocytes are busy removing the dea tissue remaining, capillaries are throwing out new loops, and the fixe tissue cells are dividing up and forming fibroblasts. Eventually ther is more or less return to the normal, but some scarring is left becaus there has been definite tissue loss, which can only be replaced, in par at any rate, by cicatricial tissue. In some large ulcers it may b possible to see all three stages in progress simultaneously, areas o spread, of balance, and of healing being found side by side.

The transitional stage may be prolonged, or healing, after beginning, may cease; the ulcer then adopts characters associated with th special accidental circumstances present. Thus it may be too larg in extent for healing to become complete: the granulation tissu becomes converted into scar tissue in the peripheral part of the woun before the whole surface has been covered by the advancing epithelium the vessels traversing it and carrying blood to the growing edge ma be compressed by this newly formed fibrous tissue beyond their capacit of maintaining the supply necessary for nutrition. When this happen the margins and floor of the ulcer become hard and sclerosed, and th ulcer is said to be "callous." Sometimes, too, the granulations becom extremely exuberant; they rise above the level of the surroundin skin, and the epithelial margin cannot spread over the raised portion Again, contraction of the base of an ulcer may be prevented b adhesions to underlying bone.

Varicose ulcers very often become stationary and callous; th surface loses its fine granulations and becomes flabby and often dirty the edges are raised and hard and show a layer of white heaped-u epithelium. There are other factors in preventing the healing o varicose ulcers, because intractable ulcers may occur without varicos veins, and varicose legs do not always become ulcerated. Leg ulcer are much commoner in women; probably two events tend to induc this greater incidence—pregnancy, because it leads directly, and i many cases permanently, to varicosity of veins; and parturition, becaus a mild post-partum streptococcal infection may extend to the ilia and femoral lymphatic glands, thereby causing a lymph blockage not sufficiently great to be recognized as "white leg," but sever enough to induce œdema of the legs after prolonged standing or walking. Stagnation of lymph or of venous blood interferes with tissu nutrition sufficiently to permit an intractable infection of low virulenc through any small abrasion; eczema and ulceration follow, and th ulcer becomes stationary, largely from a defective immunity reaction the active organism is probably in most cases a streptococcus. Aroun

stationary ulcers is found a solid chronic œdema such as is known elsewhere to be due to streptococcal activity.

The healing of ulcers has been investigated by Carrel and Leconte du Noüy. These experimenters have shown that when repair takes place normally, the rate of healing may be expressed by a mathematical formula. As the ulcerated area diminishes, so does the rate of epithelialization and contraction. The actual stimulus leading to healing of a wound or ulcer is not quite clear. Carrel, by taking extreme precautions to prevent any irritation of experimentally produced ulcers, has shown that healing, in these circumstances, is not inaugurated. But repair immediately follows mechanical irritation by a dressing or mild infection with the staphylococci always present in the skin; indeed Carrel suggests that this infection is a determining factor in initiating reparative changes.

Clinical features.—1. During the *stage of active ulceration* the surface is covered with inflammatory lymph, sloughs, and tissue in process of necrosing; granulations are absent, the edges are well-defined and sharp-cut, often irregular and "mouse-eaten." The base is thick and infiltrated. True pus is absent or slight in amount, but there is a copious, thin, perhaps blood-stained discharge which may be very offensive in odour and irritating to surrounding skin.

The neighbouring tissues are inflamed; near the ulcer the skin is reddened, infiltrated and thickened; farther out the subcutaneous tissue is often œdematous.

2. During the *stage of transition* the blood supply improves, infection becomes inactive, and sloughs are removed. The surface looks cleaner and is now glazed with a cellulo-fibrinous exudate. Sloughs are easily loosened, and granulations begin to make their appearance. The base is less infiltrated and is looser on subjacent tissues. The edges are less clean-cut and are softer. The discharge is thicker, less abundant, not sanious and less offensive. The surrounding tissues are more pliable, and are rosy; there is a quicker return of colour into a part temporarily rendered anæmic by pressure than in Stage i.

The healing stage should follow this stage, but may be postponed, and the ulcer may then fall into one of the following types:—

(*a*) In a *callous or indolent* ulcer the surface is dirty yellow, glistening and smooth, with few and flabby granulations. The base is strongly adherent to underlying tissues, such as bone, which may show periostitis or even ulceration. Great sensitiveness to pressure and spontaneous pain, worse on standing and at night, may accompany diffuse periosteal overgrowth. The edges are hard, sharp and raised. The surrounding skin may be blue and congested, brown and pigmented, sodden or eczematous. It is often heaped up at the edge. The dis-

charge is serous or purulent; it may be abundant, and may be irritant and cause surrounding eczema. The foot and leg may show pseudo-elephantiasis.

(b) A *varicose* ulcer is of the callous indolent type, with the addition of congestion due to the varicose veins; in contradistinction to syphilitic ulcers, which tend to be multiple, rounded, and on the upper and outer side of the calf, varicose ulcer is usually single and on the inner, lower part of the calf.

(c) An *irritable* ulcer is a callous ulcer in which living nerve-fibrils are exposed. It may cause severe shooting, burning pains, especially at night, and points of exquisite tenderness can be found with a probe. It is especially found near the ankle.

3. In the *healing stage* the granulation tissue becomes fibrous cicatricial tissue, and the epithelium grows over it as a fine pellicle extending in from the edges. The part as yet uncovered is smooth and shows painless red granulations, full of blood but not engorged.

The edges gently shelve; in the epithelializing areas there is an outermost white zone of new skin, a middle bluish zone several cells in thickness, and an innermost transparent zone in which red granulations can be seen through an exceedingly thin epithelial pellicle.

A *weak* ulcer is one in which the granulations, at first healthy and red, become pale, watery, flabby and exuberant; the degeneration may be caused by excessive use of ointments or wet dressings, by local poverty of nutrition perhaps due to varicose veins, or by general ill-health.

In all cases where ulcers fail to heal, the general health must be investigated, for chronic interstitial nephritis, diabetes, weak cardiac action, and general infection all inhibit the healing of wounds. Epithelioma may supervene on the margin or scar of a very persistent stationary ulcer.

Diagnosis.—Certain specific ulcers have characteristic appearances. Thus, the margin of a *syphilitic* ulcer is punched out; it is made up of segments of circles, and its sides run steeply down to the base, which is covered by the yellow wash-leather slough.

A *tuberculous* ulcer has a thin, undermined, bluish-coloured edge. The surface of the ulcer is covered by pale œdematous granulations. The discharge is thin and watery, containing shreds of tissue and tubercle bacilli.

Actinomycotic ulcers are surrounded by a great deal of indurated tissue. They have bluish-red edges, and in the discharge are the characteristic sulphur granules.

Neurogenetic ulcers occur in association with tabes dorsalis, and then they are found on the sole of the foot, or with syringo-myelia, when they may occur either on the foot or the upper limb, more often

the latter. A peripheral neuritis is liable to be associated with trophic ulcers in the area supplied by the injured nerve. The typical ulcer of tabes dorsalis occurs on the plantar aspect over the head of one of the metatarsal bones. It is perfectly painless and surrounded by a thick white cornified epithelium. *This ulcer very often leads straight* down to carious bone, which can be felt with a probe without the patient being in the least aware of the manipulation.

Malignant ulcers are recognized by the fact that they are associated always with some new formation. The bases of these ulcers are dirty and sloughy and devoid of granulations, and the edges show no epithelial activity. Repair does not take place.

Treatment.—The treatment of simple ulcers reduces itself to the removal of the cause, the combating of infection, the prevention of reinfection, the elimination of sources of irritation of the denuded surface, and the improvement of the lymph- and blood-circulation through the site of the injury.

Mechanical irritation is removed by putting the injured part at rest and by the application of a protective dressing. Improvement of the circulation is brought about mainly by posture. Infection is overcome by the established methods of treating septic wounds (*see* pp. 279, 281, 282). Especially is the Wright hypertonic saline method useful until sloughs have vanished and the wounds have become covered with red granulations. After this it is directly harmful to persist in the application of hypertonic salt solution, for this destroys the leucocytes, which are the body's defence against streptococci. At this stage a mild antiseptic ointment, such as ung. eucalypti, ung. hydarg. ox. flav., or ung hydarg ammon. dil., 10 grains to 1 ounce, should be applied.

Leg ulcers present special problems in treatment. In these the elevation of the leg to improve the circulation has a great influence on the healing. The blood- and lymph-flow can be aided by elastic pressure in several ways.

One method, as soon as the ulcer is clean enough, is to cover it with zinc plaster. To get good results by this method, it is better to apply the strapping to the whole of the leg from the foot to the knee.

In the ambulatory treatment of leg ulcers Unna's plaster is very useful. The formula is as follows:—

℞ Zinci oxidi	3 partes
Gelatini	3 ,,
Glycerini	5 ,,
Aquæ	9 ,,

A single layer of gauze bandage is wound round the limb from the foot to the knee and is painted over with the melted plaster; the

procedure is repeated until three, four, or five layers have been applied. The plaster sets and forms an elastic flexible support to the veins. It should be renewed every seven to ten days.

When the granulations become too exuberant and rise above the surface of the surrounding skin, the zinc oxide adhesive method of treatment is useful. Straps of the plaster ¾–1 in. wide are ranged along the edges of the wound, half the width being on the skin and the other half lying on the granulations. The rest of the wound is covered with ointment spread upon gauze The strapping is left on for twenty-four hours. It is only used on alternate days, the wounds being dressed with simple ointment on the intervening days. The application of the silver nitrate stick will also keep down the excessive growth of granulation tissue.

Elastic stockings are useful when new, but soon become inefficient through stretching. Martin's pure rubber bandage is convenient in that it can be washed easily, but is undesirable because it is impervious to moisture The crêpe bandage is simple, effective, and cheap, and, next to strapping or Unna's paste, is the best means of supporting the distended veins.

In the ambulatory treatment of varicose ulcers the patient should be urged to seize every opportunity to aid the circulation through the limb by posture. Whenever he is sitting, he should rest his legs upon another chair. Prolonged standing should be avoided.

Irritable leg ulcers are a source of great pain and discomfort. Careful examination with a probe will show that there are one or more exquisitely sensitive points on the surface. These areas should be painted with liquid carbolic acid or touched with silver nitrate, a measure which nearly always brings relief.

Where varicose veins are the prominent factor in the persistence of leg ulcers, they may be removed with some prospect of assisting healing. The operation should not be carried on in the close vicinity of the ulcer, from fear of infection.

Callous ulcers, especially those adherent to underlying bone, are extremely difficult to cure. Much may be done with skilful massage to free the base, to improve the nutrition, and to facilitate the removal of effete products. Two procedures which have met with a certain measure of success in the hands of some surgeons are the undermining of the edges and the making of radial incisions in their margins. When the ulcer is of any size, it is better, however, to cover it with a skin-graft. Reverdin grafts "take" the most certainly, but a pedicle flap is better. This may be got from the opposite thigh, which is maintained in apposition with the affected leg by plaster bandages until it is safe to divide the pedicle. Before performing such an operation, care should be taken to ascertain whether the

proposed position will be tolerable for the patient. The acutely bended knee, for example, may become very irksome and painful to a middle-aged patient, and he may be unable to maintain the position long enough for a pedicle graft to be made. If pedicle-grafting be performed, the resulting surface is far more capable of resisting injury. Whole-thickness Wolff grafts can be used when, for any reason, pedicle-grafting is contra-indicated. The prospect of success with this m.thod of grafting is much less than after the Reverdin method or the pedicle method. The resulting skin surface, however, is very good. Thiersch grafts may also be used with success.

Stimulants to epithelial growth, such as scarlet-red (amido-azo-toluol) ointment, have been abandoned. The incitement to epithelial proliferation is more than counterbalanced by the harmful irritation produced. If scarlet-red be used, it should be applied as an ointment not stronger than 4 per cent.; the lint smeared with it should be cut to the shape and size of the ulcer, and surrounding skin should be protected with zinc ointment.

Specific infective ulcers, besides general methods of treatment, require special remedial measures. This applies to syphilitic, tuberculous, actinomycotic, and tropical ulcers, and the lesion resulting from infection with anthrax.

Trophic ulcers usually remain unhealed under ordinary methods of treatment. Chipault devised the method of nerve-stretching for such ulcers, and claimed success He has been supported in his claim by other surgeons, though there have been some reports of failures. As the ulcer is usually on the sole of the foot, the plantar nerves require stretching. They are exposed by an incision behind the internal malleolus. Nerve-stretching has also been recommended for irritable leg ulcers, and even for simple varicose ulcers. In this case, either the internal saphenous nerve or the external popliteal will need stretching. Too much force should not be used in dealing with the latter nerve, or muscular paralysis may result. At the same time that the nerves are stretched, a trophic ulcer should have its walls and floor thoroughly scraped and disinfected with pure carbolic acid. Curetting a leg ulcer will also sometimes stimulate repair. Finally, in trophic ulcers associated with a peripheral nerve injury, healing may sometimes be induced by carefully cleaning the main vessel of the limb for about one inch so that all the accompanying branches from the sympathetic are divided.

GANGRENE

BY CYRIL A. R. NITCH, M.S., F.R.C.S.

Definition.—Gangrene is the term employed to denote the death of portions of the body sufficiently large to be visible to the naked eye; for example, a finger, a toe, a part or the whole of an extremity, or a portion of the soft parts. Death of a small part of the body, limited to the soft parts, is usually described as sloughing, while death of bone or cartilage receives from clinicians the special and more accurate designation of necrosis.

Inflammation and gangrene.—Inflammation is sometimes a prominent factor in the etiology of gangrene in that it may lead to the essential cause of gangrene—viz. failure of the circulation. One of three terminations of the inflammatory process is possible: resolution may take place owing to cessation of the cause of inflammation, granulation tissue may be formed by its continuance, or extensive thrombosis ending in gangrene may be induced by its violence. Necrosis of bone, a common form of gangrene, usually a result of inflammation, serves to emphasize the importance of the rôle occasionally played by inflammation in the production of gangrene.

Again, it is by an inflammatory process that the line of demarcation is formed whereby the dead part is separated from the living. The incidence of this process may be directly responsible for the extension of the gangrene, particularly in the senile variety, in which there is lowered vitality of the part consequent on the small calibre of the blood-vessels.

GENERAL OUTLINE OF THE PROCESS

A formal classification of gangrene will be found at p. 238, and subsequently the different varieties are fully discussed under their respective headings. At present, to avoid repetition, it may merely be pointed out that clinically there are two forms—*dry gangrene* and *moist gangrene*—and that the moist variety is distinguished as either septic or aseptic. Whether a case will be dry or moist is largely a matter of accident, and depends, among other factors, upon the

conditions which regulate the amount of fluid in the tissues at the time of their death. If the return of venous blood is impeded in any way—either by the sudden cessation of the propulsive force exerted by the arterial stream, as in the case of embolism, or by definite mechanical obstruction to the venous circulation, as in strangulation of the intestine—the affected part will be loaded with fluid, and the immediate condition will be that of aseptic moist gangrene. If micro-organisms now gain access to the part, or if they were already present at the time of death, putrefactive changes will rapidly set in, and the condition will be that of septic moist gangrene. However, should the evaporation of fluid be promoted, the return circulation favoured, and the part kept strictly clean, the area of aseptic moist gangrene may be partially or totally converted into dry gangrene.

In order to elucidate the foregoing statements, it will be advisable *to discuss these clinical forms of gangrene at greater length.*

Dry gangrene.—This form is usually due to the arrest of the arterial blood supply to tissues which are drained by an efficient venous circulation. It occurs in superficial parts of the body which are freely exposed to the air, so that desiccation is aided by evaporation. The gangrenous process spreads very slowly, for, owing to the dryness, putrefactive changes due to invasion by saprophytic bacteria are rendered difficult or impossible. The classical example of dry gangrene is senile gangrene of the extremities (Fig. 9), which is generally

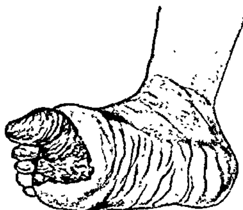


Fig. 9.—Case of dry gangrene (senile), The process had gone on for about eight weeks before the photograph was taken.

met with in association with endarteritis, whereby the calibre of the blood-vessels *is diminished. But it must* be remembered that dry gangrene may occur in a limb in which the principal artery, though healthy, is suddenly blocked by an embolus or a ligature, provided that the venous circulation is unimpaired, that

evaporation is favoured, and that saprophytic micro-organisms are rigidly excluded. Prior to actual death, numbness and tingling, followed later by acute pain, are felt in the affected part. The pain is due partly to neuritis, partly to an impaired blood supply to the nerves; and it generally persists until the gangrene is well established, because the axis-cylinders are the last to die. Cessation of pulsation in the vessels is followed by loss of heat, loss of tactile sensation, and loss of function. The skin, at first waxy in colour, becomes greasy, transparent, and yellow, owing to liberation of fat from the tissues and alteration in the hæmoglobin, and finally turns black. The dead part is now shrivelled, hard, and dry, and usually emits a peculiar musty odour.

The minute changes which immediately precede the death of the tissues cannot be described, as the particular detail or substance of the living cell that disappears or changes at the moment of death has never been isolated chemically nor seen under the microscope. But in necrotic cells, according to Hektoen and Riesman, "the nucleus very soon becomes indistinct, due either to an apparent solution of the chromatic substance, known as karyolysis or chromatolysis, or to a breaking-up of the nucleus into a number of irregular fragments, a form of disintegration which Schmaus and Albrecht have shown is initiated by a peculiar transposition of the chromatic filaments. At times the nucleus, together with the cell body, changes into a hyaline mass. The cytoplasm of necrotic cells loses its normal granulations and undergoes hyaline transformation, or vacuolation. The exact chemical processes that underlie these changes in necrosis are not known. In many instances the factors necessary for the precipitation of fibrin are present, giving rise to the so-called coagulation necrosis" Fat-globules escape from their cells and infiltrate the tissues, rendering them greasy and more or less transparent, while necrosis of the red blood-corpuscles allows their hæmoglobin to escape and stain the part brown or black. When the necrotic process ceases, the dead part acts as an irritant, and the living tissues immediately in contact with it become inflamed and pass through the series of changes leading to the formation of granulation tissue A line of separation in the form of superficial ulceration now forms This gradually deepens, until finally the dead part is completely separated and drops off, leaving on the living part an ulcer which heals by cicatrization. Hæmorrhage during the process of separation is prevented by thrombosis, which subsequently leads to the permanent occlusion of the vessels

In the early stages constitutional symptoms are slight, and, beyond the inconvenience arising from a part being insensitive and functionless, the patient complains of little more than occasional shooting

pains or numbness and tingling in the affected area. As the gangrene develops, *pain* and *toxæmia* become prominent *symptoms*, and lead to loss of sleep and gradual exhaustion, which may end in death. *Glycosuria* is a frequent accompaniment of this form of gangrene, and is due to lowering of the sugar-saturation point of the blood by the absorption of toxic products from the dead and dying tissues. *It must* not be mistaken for the glycosuria of diabetes, for it is unaccompanied by the classical symptoms of that disease, and passes off when the dead part is removed

Moist gangrene is the term employed to denote dead tissues which are infiltrated with blood and other fluids, and usually infected with saprophytic micro-organisms. It occurs in its most typical form when a necrotic part of the body becomes the seat of decomposition, and usually develops in tissues that are naturally exposed to bacterial infection, such as the lungs, the intestines, the external genitals, and the extremities. The *predominant factors in its causation* are: (1) mechanical obstruction to the venous as well as the arterial circulation, such as is produced by crushing or long-continued pressure, or by ligation, destruction, embolism or thrombosis, of a main artery or vein, or both, when the collateral vessels are diseased and therefore incapable of responding rapidly to the sudden strain thrown upon them; (2) chemical irritants and physical agents, such as heat or intense cold; and (3) the destructive action of the toxins produced by septic and infective micro-organisms which are either present before death, or subsequently gain access to the part.

Though the essential features of moist gangrene are due to putrefactive changes which occur in the necrotic tissues, decomposition does not invariably take place; hence *clinicians now recognize two distinct* forms, *aseptic moist gangrene* and *septic moist gangrene*.

Aseptic moist gangrene, or moist gangrene without putrefaction, occurs when the return of venous blood is prevented by any of the causes already mentioned, and when saprophytic bacteria fail to gain access to the part. The necrotic tissues become *sodden* and discoloured owing to the escape of blood from the vessels and *the liberation of hæmoglobin.* Later, blebs containing blood-stained serum form beneath the epidermis, the skin exhibits a play of colours ranging between dark-red, purple, green, and black, and the part becomes cold, insensitive, and functionless. If the obstruction is arterial alone, the skin is at first white, and later becomes mottled, while the course of *the superficial veins is indicated by* a dusky line due to the escape of hæmoglobin, but if the venous circulation is also interfered with, the part at once becomes dark and œdematous, and bullæ rapidly appear. The affected area remains stationary in size, a line of separation forms, and the part is cast off with very *little*

evidence of inflammatory disturbance. The process is a rapid one, because the circulation is interrupted suddenly, and a large area of the body is frequently involved.

Occasionally, however, if evaporation is assisted, and drainage of the part promoted, either by elevation or by establishment of a collateral circulation, no matter how feeble, aseptic moist gangrene may be converted into dry gangrene. Subjective symptoms are limited to pain, which may be very acute if embolism be the cause of the gangrene Though constitutional symptoms are generally slight, there may be a mild degree of toxæmia from absorption of the products of tissue necrosis.

Septic moist gangrene occurs when necrotic tissues are infected with saprophytic bacteria The part which micro-organisms play in relation to this form of gangrene is a twofold one. In the first place, the toxins secreted by them may be directly responsible for the death of the tissues, as in gangrenous cellulitis due to the *Streptococcus pyogenes*, and in gas gangrene following infection of a wound with anaerobic organisms; or, in the second place, they gain access after the gangrenous process has commenced, and lead to the putrefactive changes which characterize septic moist gangrene Coincidently with the cardinal signs of necrosis, viz cessation of pulsation in the vessels, loss of heat, loss of sensation, and loss of pain, the skin (presuming that an extremity is affected) changes in colour. The amount of blood in the part at the time of death determines the primary tint If the part be anæmic, it first assumes a peculiar waxy hue; if hypervascular, it becomes dusky red and mottled in places with patches of green and purple. Bullæ, containing dark-coloured odorous fluid, form beneath the epidermis, which soon gives way and reveals a green or black slippery dermis Patches of green skin now separate at the least touch, exposing the muscles, which are seen to be falling apart and liquefying.

Meanwhile, the part has increased in size, emits a foul odour, and frequently crepitates on pressure from distension with putrescent gases. Finally, when the gangrene ceases to spread, a line of separation forms, and a slimy, fetid, many-coloured mass, consisting of disintegrated and partially liquefied soft parts, falls away, leaving the bone bare and dry.

The *minute changes* which occur may be summed up in a few words. When living tissues become the seat of a septic or infective process, the bacterial toxins induce such an excessive leucocytosis and proliferation of connective-tissue cells that extensive stasis, followed by thrombosis in the small vessels, results Continued action of the toxins, aided by *the loss of blood supply, leads to necrosis of* the tissue cells, which then undergo the changes already described

under Dry Gangrene. Hæmoglobin escapes from the red blood-corpuscles, and, infiltrating the sodden *tissues, stains them* a deep red.

The *putrefactive changes* which now commence are due solely to the action of bacteria upon dead tissues. As the process is one of oxidation and ends in the formation of carbonic acid, water, and free nitrogen, the rapidity of its performance depends upon the supply of oxygen derived from the air. If this is stinted, the intermediate products are relatively greater in number, and occupy the transition stage for a longer period. Putrefactive bacteria, such as the various forms of *Proteus*, the *Bacillus pyogenes fœtidus*, and the *Micrococcus fœtidus*, by their action upon the complex proteid molecule, lead to the formation of a variety of chemical products, nitrogenous and non-nitrogenous. The nitrogenous products are free nitrogen, free ammonia, foul-smelling bodies, indol, skatol, tyrosin, ptomaines, and albumoses; while the non-nitroger [illegible] carbonic acid, hydrogen, sulphuretted hydr [illegible] organic acids, as formic, butyric, [illegible]

Owing to the rapidity with which the gangrenous process spreads, and the number and variety of poisonous products that are formed, *constitutional symptoms are very severe, and the* gravity of the condition is accentuated when a large area of the body, or a vital organ such as a loop of intestine, is affected. The characteristic signs of septic intoxication—high temperature, rapid feeble pulse, dry brown tongue, and muttering delirium—soon develop, and, even though energetic measures be adopted, death frequently takes place from exhaustion or toxæmia.

Line of separation.—In both dry and moist gangrene the dead part acts as an irritant *to the living tissues immediately* in contact with it, and in the latter form this irritative effect is increased by the presence of bacteria. In consequence, a process of inflammation varying in intensity with the character of the gangrene, and leading to the formation of a "line of demarcation," is set up in the living tissues. This progresses to the stage of granulation, when the proteolytic action of leucocytes and bacteria leads to cell necrosis, liquefaction, and suppuration. A line of ulceration circumscribing the necrotic area now appears upon the *surface; the furrow* thus formed deepens gradually until separation is completed, when *the dead* part falls away, leaving an ulcer which heals by granulation. As the line of demarcation depends upon the inflammatory reaction in the surrounding tissues, its appearance will vary in different cases.

In dry gangrene, owing to the feeble circulation in the living tissues and the absence of putrefaction in the dead, the line is *ill-defined* at first and forms very slowly. It is also very unstable, for, owing to special circumstances which *will be discussed later*, the gangrene may

spread, and the process be repeated several times before the final line of separation appears. The zone of inflammatory hyperæmia and increased warmth in the living tissues is so slight that the soft, pale, healthy skin presents a vivid contrast to the hard, dark, and shrivelled area of gangrene. As bone receives a better supply of blood than either skin or muscle, a conical stump is the usual result of spontaneous separation.

When the gangrene is moist but aseptic, the inflammatory reaction is more marked and the process of separation extends with greater rapidity, though in other respects it does not differ very obviously from the "line" that forms in the dry variety. In septic moist gangrene, however, the inflammatory zone is well defined; the living tissues are bright-red, turgid with blood, œdematous, hot, and painful, and not infrequently the inflammation and its attendant symptoms are aggravated by lymphangitis and extensive cellulitis. If all goes well, the line of separation deepens rapidly, and the dead part drops off or falls away from the bone in about ten days.

In some instances, owing to extension of the gangrenous process, a line of demarcation, together with an abortive furrow, may form several times before actual separation takes place. This extension usually occurs in connexion with dry or senile gangrene, and may be due to one of the following causes: (1) the inflammation at the periphery of the living part, even though very slight, may be relatively too severe for the anæmic tissues, which consequently succumb; (2) bacteria may gain access and lead to further necrosis; (3) the cause which led to the gangrene in the first instance may continue its action on the living tissues.

Treatment of gangrene.—Setting aside the details, which depend so essentially upon the nature and form of the gangrene that they are better discussed under their appropriate headings, the general principles of treatment, no matter what the variety of the condition, are clearly defined.

When gangrene is threatened, every possible means must be employed to render the part aseptic, by careful shaving, by thorough washing with soap and water (paying particular attention to the nails and the folds of the skin), and by enveloping it in a voluminous dressing of dry sterilized gauze and wool. Warmth must be maintained by hot-water bottles, so arranged that the part cannot come in actual contact with them; and drainage of the fluids must be assisted by the relief of any cause of constriction, by elevation, by gentle friction towards the heart, by promotion of evaporation, or by a timely incision.

When gangrene has actually occurred, the separation of the dead from the living must be assisted, or amputation must be resorted to.

General constitutional treatment must be carried out; the patient's strength must be supported by *stimulants* and *suitable nourishment*, the excretions must be regulated, pain must be relieved, and sleep encouraged.

The question of amputation, and the site at which it shall be performed, will depend upon the cause of the gangrene, the rapidity of its progress, the symptoms which accompany it, and the general condition of the patient.

When an operation is necessary, the method of inducing anæsthesia requires careful consideration. In most cases the choice should rest between gas-oxygen-ether and spinal anæsthesia.

CLASSIFICATION

It is impossible to draw up an accurate etiological classification of gangrene, owing to frequent interaction of the various causes, but the one now given, though admittedly imperfect, is based on a combination of clinical and pathological grounds and includes all the important varieties.

I. Gangrene due to circulatory disturbances.

1. Impairment of the general circulation.
2. Embolism.
3. Thrombosis.
4. Ligation of vessels.
5. Injury of vessels (indirect traumatic gangrene).
6. Pressure on vessels.
7. Disease and degeneration of vessels (senile gangrene).
8. Spasm of arterioles: Raynaud's disease. Ergotism.

II. Gangrene due to defective innervation.

1. Trophic ulcers.
2. Certain forms of bed-sore.

III. Gangrene due to injury.

Direct traumatic gangrene.

IV. Gangrene due to physical and chemical agents.

1. Heat.
2. Cold.
3. Escharotics.

V. Gangrene due to infective processes.

1. Acute inflammation.
2. Gas gangrene.
3. Cancrum oris.
4. Phagedæna.

VI. Diabetic gangrene.

I. GANGRENE AS A RESULT OF CIRCULATORY DISTURBANCES

1. Gangrene due to impairment of the general circulation seldom depends upon cardiac insufficiency alone, but rather upon a combination of circumstances which includes the condition of the arteries, the slowness of the circulation, and the nutrition of the tissues. Malformations of the heart, degeneration of its muscle, or diseases of the endocardium predispose to gangrene when the circulation is feeble, or actually cause it by liberating emboli. A patent foramen ovale, and mitral or pulmonary stenosis, predispose to gangrene because aeration of the blood is not complete. Degeneration of the cardiac muscle leads to lowered blood-pressure, feeble circulation, and capillary stasis, whereby the vitality of the tissues is so diminished that they readily succumb to pressure, to a trivial injury, or to a mild degree of inflammation. Exhausting diseases, severe hæmorrhage, starvation, and physical exhaustion act in a similar manner on the tissues, and also encourage the formation of thrombi in the vessels, particularly in the extremities, where the circulation is especially feeble

Symptoms.—This variety of gangrene has a tendency to be dry unless thrombosis or embolism of a large vessel, or any other cause of sudden and complete stasis, be the determining factor, when it is more likely to be moist The symptoms preceding its onset are usually masked by those of the disease or condition with which it is associated. Sooner or later it will be noticed that the whole or part of a limb, possibly only the tip of a digit or the lobe of an ear, has become cold, pulseless, and insensitive; or, if much fluid be present, local death is heralded by dusky-red, indurated patches surmounted by blebs containing sanious fluid The onset of gangrene in these cases is usually a terminal sign, is often symmetrical, and is soon followed by the death of the patient.

Treatment.—The occurrence of gangrene may be delayed or prevented by the administration of cardiac stimulants, by inhalation of oxygen, by venesection when the heart's action is embarrassed, or by saline infusion when fluid is required during the stage of shock or after severe hæmorrhage. When thrombosis is feared, friction

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must be avoided lest emboli be set free, and 20-gr. doses of sodium citrate given thrice daily for the purpose of diminishing the coagulability of the blood. Warmth in the part must be maintained, and all sources of pressure avoided Surgical interference is seldom required, as the condition of the patient usually precludes recovery. If an amputation is considered advisable, it should be so planned as to be well above the seat of obstruction.

2. **Gangrene due to embolism.**—Embolism of a large artery is a frequent cause of gangrene. It acts by suddenly cutting off the blood supply from a large area of tissue whose vitality, already lowered by pre-existing cardiac disease or endarteritis, is unable to survive the temporary ischæmia, and therefore death of the part occurs before an efficient collateral circulation can be established. Without doubt, disease of the small vessels and arterioles, leading to a diminution of their calibre, is the most important factor in the production of gangrene of the extremities following the sudden interruption of the arterial circulation, whether it be due to embolism, thrombosis, or ligation; for, in the limbs at all events, the anastomotic circulation is usually sufficient to maintain life, provided the small vessels are of normal size and resilience. This is proved by the number of times that the external iliac, the common femoral, and the axillary arteries have been ligated with impunity. Embolism is more frequent in the old, but may occur at any age. Emboli, though usually associated with organic disease of the heart, when they arise from vegetations on the valves or from coagula in its cavities, are sometimes composed of calcareous plates that have been dislodged from an atheromatous artery; they are usually arrested at the bifurcation of a large vessel, particularly in the lower extremity.

Symptoms.—The immediate effect of an embolus is intense pain at the site of its arrest—a most valuable sign, inasmuch as it points to the cause and position of the obstruction The flow of arterial blood ceases, and the skin becomes white; later, as the collateral circulation develops, it regains its colour over an area corresponding to the distance the blood has permeated. If the anastomotic vessels dilate rapidly enough the part will recover completely, but if there be delay in the re-establishment of the circulation a portion or the whole of it will die. As there is no obstruction to the return of venous blood, the gangrene is usually dry. If drainage of the blood in the necrotic area be defective the skin becomes dusky red, bullæ form on the surface, and the changes which characterize moist gangrene follow rapidly. This may remain aseptic throughout, but if the embolus has been formed by an infective vegetation in the first instance, or if, as is only too probable, bacteria gain access from without, signs of putrefaction will develop quickly.

Treatment.—The limb must be thoroughly cleansed, enveloped in sterilized wool and bandages, and elevated as soon as possible. By the employment of two or three pillows for its elevation, warmth is maintained and pressure evenly distributed. The extent of the gangrene will be evident in two or three days. As a rule, a considerable portion of the limb below the embolus will recover; hence it is always advisable to wait for at least forty-eight hours before adopting radical measures. As there is no necessity to wait for a line of separation unless the toes alone are affected, amputation should be performed as soon as the limit of the gangrene is defined. The site will be determined by the anatomy of the vessels and the extent of the collateral circulation.

Generally speaking, when gangrene is due to embolism or thrombosis, the section of the limb should be made above the seat of obstruction. This applies especially to the popliteal artery, for the anastomosis between the profunda femoris, the anastomotica magna, and the tibial arteries is rarely sufficient to nourish the tissues below the knee. In cases of femoral embolism, amputation below the block may be attempted; but if during the operation there be but little hæmorrhage, a higher amputation must be performed immediately. When embolism is followed by moist gangrene, immediate amputation above the seat of obstruction is always indicated.

3. Gangrene due to thrombosis.—Thrombosis may occur either in an artery or in a vein, or simultaneously in both.

Arterial thrombosis is generally due to disease, especially endarteritis, atheroma, and acute arteritis. It usually follows injury when the tunica intima is bruised or torn, and always accompanies embolism. In various infective and wasting diseases, such as typhoid, typhus, puerperal, and scarlet fevers, pneumonia, and acute rheumatism, arterial thrombosis, with or without venous thrombosis, has been the forerunner of gangrene. In many instances it is suggested that embolism of the vasa vasorum leads to endarteritis and its resulting thrombosis. The vessels most often affected are, in the order of frequency, the aorta, the femoral, the popliteal, and the common iliac arteries.

Venous thrombosis alone is rarely the cause of gangrene, even when an important vein is occluded, for the number of superficial and deep veins is so great, and their anastomoses are so free, that there is always some channel by which the blood can return. Though the only obvious cause of gangrene of the lower extremity occurring during the course of typhoid fever has been thrombo-phlebitis of the femoral vein, it is highly probable that other conditions, in the form of general debility, toxæmia, and a sluggish circulation, have been the real determining factors. On the other hand, venous thrombosis following

pressure due to prolonged application of a tight bandage or a tourniquet, or to a rapidly growing tumour or a large aneurysm, is usually followed by moist gangrene because the majority, if not all, of the veins are obliterated. Simultaneous thrombosis of an artery and a vein, though occasionally resulting from any of the causes of thrombosis already mentioned, more often follows a severe injury like the passage of a cart-wheel across a limb, when the coats of the vessels are extensively damaged or torn.

Symptoms.—The signs of gangrene due to *arterial thrombosis* develop slowly, and are generally ushered in by certain premonitory symptoms. The limb aches, power diminishes, pain and cramps, followed by rigidity, are experienced in the muscles, and soon the limb becomes cold, pulseless, and paralysed. The blanched skin is marbled in places with patches of red, and the course of the veins is mapped out by dusky lines. An area of dry gangrene, depending upon the extent of the collateral circulation, now develops, and if left would in time be cast off in the usual manner. When necrosis is due to *venous obstruction* alone, or to both arterial and venous obstruction, the skin, instead of being white, becomes œdematous and dusky-red from congestion, blebs form on the surface, the epidermis peels off, and moist gangrene sets in.

Treatment.—When the gangrene is due to *arterial thrombosis*, the rules already laid down for the treatment of embolic gangrene hold good; but when arterial thrombosis is complicated by *venous obstruction*, or when venous thrombosis exists alone, an amputation above the level of the lesion should be performed as soon as possible.

4. **Gangrene due to ligation of vessels.**—Ligature of the main artery rarely causes gangrene in a limb, because the collateral circulation in healthy vessels, no matter how feeble, is generally sufficient to maintain life until the arterioles have accommodated themselves to the altered conditions. If, however, the vitality of the tissues is already lowered by exhausting diseases, or if the peripheral and collateral vessels are narrowed by endarteritis or calcareous degeneration, dry gangrene of limited extent is likely to occur. Before the War it was considered that moist gangrene was very prone to follow simultaneous ligation of both artery and vein, but in 1915 Sir George Makins pointed out that occlusion of both vessels, *in healthy adults free from arterial disease*, is less liable to be followed by gangrene than ligation or excision of the artery alone—the explanation being that if the main vein is patent the limb is quickly drained of its blood before the collateral circulation becomes sufficiently large to nourish the tissues. Therefore by ligation of the main vein a balance is struck between a feeble collateral circulation and a rapid venous return When ligation in continuity is performed for the

cure of aneurysm, the conditions are somewhat different. Proximal ligature of both vessels close to the sac, by Anel's method, is usually free from danger; but the Hunterian operation, or proximal ligature at a distance from the sac, should it succeed in curing the aneurysm, places a double block upon the circulation, one at the site of ligature, and one at the clotted aneurysm; consequently, the life of the part below the sac depends upon the dilatation of two distinct sets of collateral vessels.

The symptoms and treatment in general are so similar to those of embolic and thrombotic gangrene that repetition is unnecessary. One detail of treatment, however—the site of amputation—requires discussion. It is not always necessary to amputate at the level of the ligature if the artery alone is occluded, as an efficient collateral circulation will nourish the tissues for a considerable distance below. This is especially noticeable when the superficial femoral artery is tied, for the profunda will easily rise to the occasion and supply the limb as far as the knee. Hence a knowledge of the anatomy of the arteries, and the exercise of a little patience in waiting for a collateral circulation to develop, will often permit of an amputation considerably lower than the seat of obstruction.

5. Gangrene due to injury of vessels.—This form is sometimes spoken of as *indirect traumatic gangrene*, because the tissues which die are generally at a distance from the seat of the injury.

Railway accidents, cart-wheel crushes, bullet wounds, fractures, etc., cause injuries to the vessels of varying severity. In the first place, a slight contusion may cause a simple plastic endarteritis or endophlebitis which will be followed by thrombosis; secondly, an injury of greater severity may lead to rupture of the intima alone, when thrombosis and complete occlusion of the vessel will ensue; thirdly, the vessel may be ruptured or completely divided, and the effused blood, by collecting in the tissues, so compresses the neighbouring vessels as to complete the obstruction; fourthly, a displaced fragment of a fractured bone may lacerate a vessel, or so compress it as to stop the circulation in it; and fifthly, the violence may be so severe that every structure in the limb at the site of its application is immediately destroyed. (*See* Direct Traumatic Gangrene, p. 251.)

Symptoms.—The form of gangrene that develops depends entirely upon the nature of the injury, the vessel or vessels that are damaged, and the presence or absence of septic infection. If the main artery alone is damaged, pulsation in the vessel ceases abruptly at the site of injury, and the limb below becomes pallid, cold, insensitive, and functionless. Within twenty-four to forty-eight hours, provided that extravasation of blood is slight or absent, the collateral circulation develops, and complete recovery ensues or dry gangrene commences

pressure due to prolonged application of a tight bandage or a tourniquet, or to a rapidly growing tumour or a large aneurysm, is usually followed by moist gangrene because the majority, if not all, of the veins are obliterated. Simultaneous thrombosis of an artery and a vein, though occasionally resulting from any of the causes of thrombosis already mentioned, more often follows a severe injury like the passage of a cart-wheel across a limb, when the coats of the vessels are extensively damaged or torn.

Symptoms.—The signs of gangrene due to *arterial thrombosis* develop slowly, and are generally ushered in by certain premonitory symptoms. The limb aches, power diminishes, pain and cramps, followed by rigidity, are experienced in the muscles, and soon the limb becomes cold, pulseless, and paralysed. The blanched skin is marbled in places with patches of red, and the course of the veins is mapped out by dusky lines. *An area of dry gangrene, depending upon the extent of the collateral circulation, now develops, and if left would in time be cast off in the usual manner.* When necrosis is due to *venous obstruction* alone, or to both arterial and venous obstruction, the skin, instead of being white, becomes œdematous and dusky-red from congestion, blebs form on the surface, the epidermis peels off, and moist gangrene sets in.

Treatment.—When the gangrene is due to *arterial thrombosis*, the rules already laid down for the treatment of embolic gangrene hold good; but when arterial thrombosis is complicated by *venous obstruction*, or when venous thrombosis exists alone, an amputation above the level of the lesion should be performed as soon as possible.

4. **Gangrene due to ligation of vessels.**—Ligature of the main artery rarely causes gangrene in a limb, *because the collateral circulation in healthy vessels, no matter how feeble, is generally sufficient to maintain life until the arterioles have accommodated themselves to the altered conditions* If, however, the vitality of the tissues is already lowered by exhausting diseases, or if the peripheral and collateral vessels are narrowed by endarteritis or calcareous degeneration, dry gangrene of limited extent is likely to occur. Before the War it was considered that moist gangrene was very prone to follow simultaneous ligation of both artery and vein, but in 1915 Sir George Makins pointed out that occlusion of both vessels, *in healthy adults free from arterial disease*, is less liable to be followed by gangrene than ligation or excision of the artery alone—*the explanation* being that if the main vein is patent the limb is quickly drained of its blood *before the collateral circulation becomes* sufficiently large to nourish the tissues. Therefore by ligation of the main vein a balance is struck between a feeble collateral circulation and a rapid venous return. When ligation in continuity is performed for the

cure of aneurysm, the conditions are somewhat different. Proximal ligature of both vessels close to the sac, by Anel's method, is usually free from danger; but the Hunterian operation, or proximal ligature at a distance from the sac, should it succeed in curing the aneurysm, places a double block upon the circulation, one at the site of ligature, and one at the clotted aneurysm; consequently, the life of the part below the sac depends upon the dilatation of two distinct sets of collateral vessels.

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at the periphery. If the vein alone is injured, the limb below becomes dark, congested, and œdematous, and typical signs of aseptic moist gangrene may appear. Should rupture of the artery or the vein, or both, occur, the blood escapes into the tissues in such quantity that the skin appears stretched to bursting-point; cessation of pulsation below the injury is followed by considerable swelling of the limb owing to the pressure on the veins, while the skin, which is pale and bloodless at the periphery, becomes tenser and dusky-red towards the site of injury; blebs filled with clear serum rapidly form, the epidermis is easily rubbed off, exposing the derma, from which a copious exudate of bloody serum escapes. Numbness and tingling, or intense pain due to pressure, are felt along the course of the nerves. At this stage, if active surgical measures are delayed, moist gangrene, nearly always septic in character, commences and rapidly spreads up the limb, while the patient suffers with severe constitutional symptoms due to absorption of the products of putrefaction. Lastly, in those cases in which all the tissues are destroyed at the site of injury, as happens when the wheel of a heavy cart passes across the thigh, the limb below, deprived of its vascular and nervous supply, naturally dies; and as it was full of fluid at the time of the injury, the gangrene is primarily moist. The part is painless, inert, and functionless, causes no constitutional symptoms, and, if it could be kept free from putrefactive organisms, the fluid would evaporate, and it would slowly dry up and mummify. But if bacterial infection occur, putrefaction, with its attendant train of local and constitutional symptoms, will set in.

Treatment.—Immediately the case is seen, the most elaborate precautions must be taken to render the part aseptic by the means described (p. 237). The limb should be examined to determine the presence or absence of circulation and, if possible, the nature and extent of the injury. If the tissues are so severely injured that recovery of the part below is obviously impossible, amputation must be performed as soon as the patient has recovered from shock; but whenever the presence of undamaged tissues between the threatened area and the injured part leads to the hope that gangrene may not ensue, it is advisable to wait for several hours in the expectation that an efficient collateral circulation will develop. The delay is also advantageous by allowing the patient to recover from collapse which might prove fatal if the shock of an immediate amputation were superadded. If within twenty-four hours there are no signs of recovery in the part, or if gangrene has already commenced, an amputation should be performed above the site of the injury. If, however, a collateral circulation has developed, the greater part of the limb may recover and only the distal portion become gangrenous. Then,

if asepsis be maintained, and evaporation assisted, the necrotic tissues will become dry and may either be allowed to drop off or, as is usual in such circumstances, be removed by amputation, but at a much lower level than was originally anticipated. Should any source of compression embarrass the circulation at the time of injury, or during the period of waiting, an incision should be made, clots removed, hæmorrhage arrested, displaced fragments of bone replaced or fixed, and the condition of the main vessels determined. If either the main artery or vein, or both, are found to be severely injured, continuity should be restored by means of Tuffier's tubes. In this way occlusion of the vessels by thrombosis will be delayed for about twenty-four hours, by which time the collaterals will have dilated sufficiently to preserve the vitality of the whole or a greater part of the limb. The tubes are removed at a later date after ligaturing the vessels above and below the lesion. But when injury to the vessels is complicated by laceration of muscles and division of important nerves, the immediate danger of septic moist gangrene is so great, and the limb would be so useless in the rare event of its recovery, that it should be amputated as soon as the patient's condition permits.

Another matter that calls for careful consideration in deciding on the proper treatment is the age and constitutional condition of the patient. Old people seldom bear injuries well, and are often less able to undergo the strain of prolonged convalescence than the shock of an immediate amputation; while the vitality of their tissues is frequently so lowered by cardiac disease, arterio-sclerosis, or chronic nephritis, that gangrene is practically inevitable after a severe injury. Immediate amputation is therefore called for more often than in the case of younger healthy adults.

6. **Gangrene due to pressure.**—Gangrene of the extremities may be due to pressure on the vessels from a tumour, a fractured or dislocated bone, a rapidly enlarging aneurysm, or prolonged constriction with a tourniquet or a tight bandage. It may be dry, but is usually moist, for the veins, being thin-walled, are more readily compressed than their companion arteries. A case of dry gangrene from constriction is illustrated in Fig. 10. The **symptoms** are characteristic: swelling, congestion, and œdema, accompanied by intense pain from pressure on the nerves, are quickly followed by the classical signs of moist gangrene. When necrosis is threatened, **treatment** must be directed towards the removal of the cause. If complete gangrene has already occurred, immediate amputation is called for, but if it is only limited in extent and aseptic, conservative measures are justifiable, and a line of demarcation may be awaited. The treatment of gangrene following aneurysm is considered elsewhere.

Another and special form of pressure gangrene is the so-called

bed-sore. A bed-sore may be defined as a gangrenous ulcer due to *necrosis of the skin and subjacent tissues from continued pressure*, usually, but not always, assisted by dirt and moisture. Bed-sores develop (1) as the result of lowered tissue vitality in the aged and infirm who are obliged to lie in one position for a prolonged period, or in adults the subjects of exhausting diseases such as pyæmia, typhoid fever, etc.; or (2) as the result *of trophic disturbances in* patients of any age suffering from injuries or diseases of the nervous system which interfere with the integrity of the cerebro-spinal centres or the peripheral nerves. They commonly occur on the sacrum, buttocks, and heels, for these are the places usually subjected to

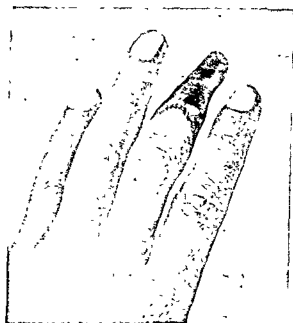


Fig. 10.—Dry gangrene of the finger in a boy of 12, following prolonged constriction by a tight bandage. (*Author's case.*)

pressure, and, *in the absence of trophic disturbances*, are caused by a process of anæmic necrosis preceded by capillary thrombosis; but if due to any nervous affection, though usually appearing in these regions, they may develop in situations far removed from any source of pressure, because vaso-motor and sensory disturbances so modify *the nutrition of the tissues* that they are unable to resist bacterial invasion.

Symptoms.—In the early stages the skin feels thicker than normal and less pliant; its colour changes to a dusky red, which does not disappear when pressure is applied, and very soon *the epidermis* separates, exposing a raw surface. If prompt measures are now taken

to relieve the pressure, recovery is possible; but if the cause is allowed to continue, or if urine and fæces contaminate the abrasion, the skin becomes gangrenous, and on separation of the slough a clean-cut ulcer with very little surrounding inflammation is revealed. Every degree of severity is met with, from a small abrasion to complete destruction of all the tissues overlying the bone. In rare cases, infective caries of the sacrum has led to death from meningitis.

Treatment.—It is customary to attribute bed-sores to bad nursing; but though the impeachment may be justified in certain cases, in others it is practically impossible to prevent their formation, especially when the patient is bedridden, and when paralysis with incontinence is present. Preventive treatment consists in varying the pressure by frequently altering the position of the patient, and distributing it by placing him on a firm, smooth mattress, a water-bed, or a ring pillow. The draw-sheet must be kept free from creases and changed whenever it becomes damp or soiled, and various devices must be employed to catch the urine when the patient is incontinent. The skin must be thoroughly washed with soap and warm water two or three times daily, carefully dried, sponged with methylated spirit or eau-de-Cologne, and powdered with a mixture of zinc oxide and starch. When a bed-sore has once formed, the separation of the slough should be assisted and the ulcer dressed with a stimulating lotion, such as sulphate of zinc 2 gr. to the ounce, until healthy granulations appear, when flavine in castor-oil, 1 : 1,000, will be found beneficial. If the patient's general condition permits of healing, the raw surface may be covered with skin-grafts; but if the conditions are not favourable, mild antiseptic or sterile dry dressings must be employed in the hope of preventing the enlargement of the sore.

7. Gangrene due to disease and degeneration of the vessels (senile gangrene).—Certain diseases and degenerative changes of arteries, leading to narrowing of their lumen and interference with their elasticity, though occasionally occurring in the young, are chiefly met with in later life. Hence the form of gangrene associated with them is known as senile gangrene. Of these, the most important are atheroma and annular calcification. Their development is due to the combined effect of a raised blood-pressure, the result of continued muscular exertion, and the circulation of the toxic products of syphilis, gout, rheumatism, Bright's disease, alcoholism, diabetes, or chronic lead-poisoning. When the changes in the vessels are due to syphilis, they are characterized by such marked hyperplasia of the tunica intima that the lumen of the small vessels may be completely obliterated. When they are arterio-sclerotic in character, the initial change is a small-celled proliferation originating in the deep layers of the intima or, according to some authorities, in the

media. In this new subendothelial tissue, which may become definitely fibrous, fatty degeneration occurs and is sooner or later followed by the formation of calcareous plaques, which, besides converting the vessel into a rigid tube unable to contract or expand, frequently project into and obstruct its lumen. *Calcareous degeneration* may occur as a primary affection of the middle coat of small arteries. Owing to the circular arrangement of the muscles in which the lime salts are deposited, it is known as *annular calcification.*

The briefest of references to the above pathological conditions will serve to emphasize the importance of arterial disease as a predisposing cause of senile gangrene. The small vessels, being converted into tortuous, rigid, narrow tubes, are unable to contract or dilate in response to the needs of the tissues, whose nutrition consequently suffers. In addition, their narrowness and tortuosity, by slowing the circulation, favours thrombosis, while the projection of calcareous plaques, or their escape into the blood-stream, determines it. Thrombosis, once commenced, is encouraged by the roughness of the intima, and may extend in an upward direction, progressively cutting off the supply of blood to distal parts. As a consequence of these altered conditions, gangrene may follow the most trivial lesion—a pin-prick, a minute [illegible] ...pody, pressure [illegible] inflammatory [illegible] than the de- [illegible] to prolonged stasis and necrosis.

Symptoms.—Senile gangrene occurs more often in men than in women, *in the proportion of about 20 to 1, is usually limited to the toes and foot,* and rarely begins before 40 years of age. Its appearance is often preceded by certain symptoms essentially due to arterial disease and its natural sequel, a defective circulation. Briefly, they consist of numbness and tingling, persistent cold unrelieved by the application of warmth, shooting pains, muscular rigidity and paresis setting in while walking and passing off with rest, and a diminution of tactile sensation which leads the patient to feel as if he were treading on cotton-wool. Examination will reveal a cold, anæmic foot with *impaired sensation that does not correspond to any particular nerve area,* and rigid tortuous arteries in which there is little or no pulsation. These premonitory signs and symptoms are of the utmost importance, for by a due appreciation of their significance it is sometimes possible to ward off an attack of gangrene. When some slight mechanical violence is applied to a toe in this condition, the skin at the site of pressure or injury turns from white to a dusky red, which does not disappear on pressure; in time this becomes [illegible] black and horny. In some cases a blister con- [illegible] *when the cuticle is removed,* [illegible] ...el and dry up, forming a hard, black patch. This patch may [illegible] ...eals, only to break down again and a [illegible] ...ted, the changes usually begin in t[illegible] ...e to the nail. Once the gangrenous process has started, it progresses very slowly, and it may be months before a line of demarcation forms. If sufficient time were allowed to elapse, this would deepen and the toe would drop off; but, *unfortunately, the process more often spreads* either to adjacent toes or along the dorsum of the foot; and a second or third line of demarcation is formed, only to suffer the same fate as its predecessor. As the more vascular tissues

can get about quite well enough with the shorter stump. Therefore the *best working rule for the treatment of senile gangrene is early amputation above the knee.*

Conservative methods of treatment of incipient or actual senile gangrene are four in number. In historical sequence they are:—

(1) *Arterio-venous anastomosis.*—The operation consists in making an axial anastomosis between the femoral artery and femoral vein in Hunter's canal, and aims at arresting the progress of the gangrene by conveying arterial blood to the tissues of the leg through the healthy veins, in order that the nutrition of the limb may be sufficiently good to allow of natural separation of the dead part, or permit an amputation at a very short distance above it. Though many cases have been reported in which a measure of success has been obtained, the writer does not consider that the results justify the risks.

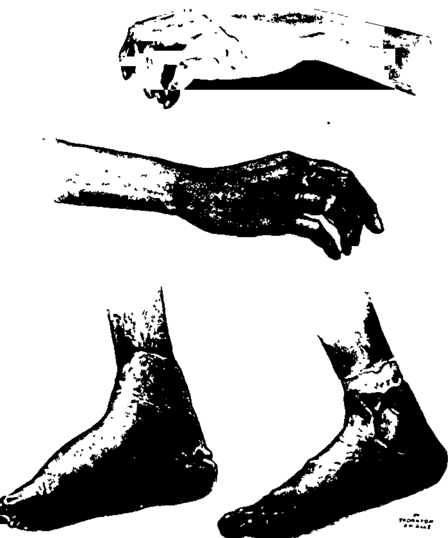
(2) *Sympathectomy* (Leriche).—The femoral artery is exposed, isolated, and denuded of its tunica adventitia (containing the sympathetic nerves) for a distance of 4 in. The immediate effect of the operation is to cause such contraction of the denuded portion of the vessel that the pulse becomes almost imperceptible and the temperature of the limb falls 3°–4° C. Within a few hours the blood-pressure and temperature rise and the vessels dilate. This vaso-dilatation begins to diminish on the fifth day, and disappears in about three weeks. The operation has been successful in Raynaud's disease and in relieving painful pregangrenous crises The initial vaso-constriction and comparatively transient vaso-dilatation therefore render this method unsuitable for established gangrene. In fact, Leriche only claims success in cases of threatened gangrene.

(3) Working on these lines, Sampson Handley has treated several cases of senile gangrene of the foot by injecting absolute alcohol (4 minims) into the tunica adventitia of the femoral artery (in Hunter's canal) at four equidistant points around its circumference. This was followed by immediate dilatation of the vessels, dramatic subsidence of the mottling on the foot, and permanent localization of the gangrene to the toes. In his preliminary communication, Handley points out that periarterial alcohol injection, besides being an easier operation than sympathectomy, has no initial constrictor effect, and that the vaso-dilatation persists for many weeks, thus rejuvenating the moribund tissues and enabling them to form a permanent line of demarcation at their junction with the dead.

(4) Recently, at St. Thomas's Hospital, several cases of senile gangrene of the toes and foot have been treated by ligature of the femoral vein in Scarpa's triangle, with results very similar to those recorded by Handley. The explanation of the improvement that follows lies in the fact that with narrow arteries and large patent veins the limb is being drained of its blood so quickly and so thoroughly that extension of gangrene is encouraged. The ligaturing of the main vein produces congestion, and so the dying tissues recover.

The beneficial effects of these two conservative methods, (3) and (4), are obvious. Either the gangrenous toes may be allowed to separate and drop off, or, owing to the improvement in the circulation, a successful amputation above the ankle can be performed.

Gangrene due to arteritis obliterans, sometimes called "pre-senile gangrene," is a form of dry gangrene occurring in persons between the ages of 20 and 50. It is essentially due to changes which commence in the small vessels and gradually spread



A rare example of bilateral dry gangrene affecting all four extremities, in a young West Indian native. The onset was sudden, and was accompanied by numbness, tingling, and pain. In the absence of any history or evidence of endarteritis, syphilis, or ergotism, the determining cause must be ascribed to Raynaud's disease. Hæmoglobinuria was probably present during the first two days. (*C. G. Choyce's case.*)

PLATE 27.

upwards, leading to obliteration of the arteries and thickening of the intima of the veins. The process is one of hyperplastic endarteritis, followed by thrombosis, and though more frequently attacking the arteries of the lower extremity, it may affect those of the upper limb alone, or arise simultaneously in both. According to Weiss, the gangrene is ultimately due to thrombosis induced by the sclerotic changes in the vessels, while Wulff regards abnormal vaso-motor constriction, analogous to Raynaud's disease, as the determining factor, and bases his hypothesis on the fact that the narrowing of the vessels in many cases has been due, not to thickening of the intima, but to hypertrophy of the muscular coat Though occasionally a sequel of syphilis, this form of endarteritis has also been ascribed to the action of cold, the abuse of alcohol and tobacco, mineral and organic poisons, and diabetes.

The **symptoms** are often characteristic. On taking exercise the patient suffers from numbness, tingling, itching, cyanosis, and weakness of the legs, which pass off again with rest; consequently the terms *intermittent limp* and *intermittent claudication* have been applied to this condition. The femoral, brachial, or subclavian arteries can be felt as hard cords, and little or no pulsation can be detected in the peripheral vessels. In due course dry gangrene sets in, involving a finger, a toe, a portion or the whole of an extremity.

Treatment in the early stages must be directed to the maintenance of warmth, the relief of pain, and the removal of any possible cause of irritation. Antisyphilitic remedies may be tried for a time, though they do not appear to have had any beneficial effect in reported cases. A gangrenous digit may be allowed to drop off, but when a foot or a hand is implicated, amputation above the knee or the elbow is usually necessary.

8. **Gangrene due to spasm of the arterioles.**—Under this heading two forms of gangrene call for description, viz. gangrene due to Raynaud's disease, and gangrene due to ergot. Gangrene caused by spasm of arterioles following cold will be discussed later (p. 255).

Gangrene due to Raynaud's disease, sometimes incorrectly termed "symmetrical gangrene," is a variety of superficial gangrene following spasm of the arterioles of nervous origin. Though generally bilateral, it may be unilateral, and even limited to the distribution of a single nerve, but it is seldom symmetrical as its oft-used synonym implies. [illegible]

were affected (Plate 27). [illegible]

arterial spasm is an ind[illegible]

neurosis; but in the majority of cases it is merely a syndrome created by some nervous affection, such as hysteria, tabes, epilepsy, syringo-

myelia, and certain forms of neuritis. When occurring as a pathological entity, the condition is not a serious one, and seldom leads to more than superficial necrosis. It is generally seen in women between the ages of 18 and 30, is often developed by cold, affects the fingers of one or both hands, and less commonly the toes, the tips of the ears, and the nose. The term "Raynaud's gangrene" should only be applied to those cases which are preceded by certain phenomena known as local syncope and local asphyxia, and which are unaccompanied by obstruction or disease of the main arteries.

Symptoms.—*Very often, as the result of some mental shock, or* under the stress of intense emotion, the fingers become pale, bloodless, insensitive, and shrunken, owing to contraction of the arterioles (*local syncope*). In time the spasm is followed by relaxation, and the digit becomes warm, hyperæsthetic, and, owing to the extremely sluggish circulation, so deeply congested as to be almost black (*local asphyxia*). These attacks occur more often in the winter, and, apart from hysterical manifestations, may start during or after a meal, when getting up in the morning, or when the patient is tired. If recovery is incomplete between the paroxysms the duskiness of the fingers continues for some days, the pain increases, small sanious blebs form, and at first sight it appears as if several fingers were about to die. Ultimately, however, the circulation gradually improves, the normal colour returns, and only a small area of skin and subcutaneous tissue becomes gangrenous and is cast off as a dry, black slough The whole process is so slow that weeks or months may elapse before separation is accomplished. The condition occasionally simulates senile gangrene and so may give rise to difficulties in diagnosis, but if it be remembered that Raynaud's disease is generally bilateral, is limited to the skin and subcutaneous tissues, affects several digits, attacks the fingers more often than the toes, and is unassociated with arterial disease, a mistake is not likely to occur.

Treatment.—When gangrene is threatened, local treatment consists in soaking the fingers in tepid salt water, drying them thoroughly, and wrapping them up in cotton-wool or thick woollen gloves. Necrotic patches must be enveloped in dry aseptic dressings and allowed to separate naturally. General constitutional treatment should be directed against the disease, and opium may be given in small doses for the relief of pain. Cases of Raynaud's disease affecting the hands alone have been recorded in which the symptoms have been ameliorated by stretching the median and ulnar nerves; but *this line of treatment is, of course, only suitable when the disease is* independent of an organic lesion. (*See also* the conservative treatment of senile gangrene, p. 250.)

Gangrene due to ergot.—The prolonged ingestion of bread made from rye infected with the *Claviceps purpurea* leads to tonic contraction of the peripheral arterioles, degeneration of their inner coats, thrombosis, and dry gangrene. Ergotism is now very rare, and practically limited to Central and Eastern Europe. It is liable to occur in cold wet summers (climatic conditions that favour the growth of the fungus), and mainly affects the poorer agricultural classes, who are often obliged to live on bread made of the diseased grain that cannot be sold. Middle-aged men appear to be peculiarly susceptible to the poison, and develop gangrene more often than women and children, owing to premature arterio-sclerosis from hard work or chronic alcoholism.

Symptoms.—The early signs of ergotism are manifested by disturbances of the central nervous and digestive systems. Giddiness, *buzzing in the ears, blurred vision, numbness, tingling, and hyperæsthesia* are accompanied by attacks of diarrhœa and vomiting; later, spasm of the muscular arterioles causes painful burning cramps, defective circulation, and coldness of the extremities. At this stage gangrene due to peripheral thrombosis is very apt to occur. It is usually of the dry type, often bilateral, generally affects the toes and feet, although the fingers, nose, and ears may be attacked. The process is so slow that one or two years may elapse before the dead part separates, while the amount lost varies from a digit to the greater portion of an extremity.

Treatment.—The premonitory symptoms, if recognized, may be relieved and the gangrene prevented by cutting off the supply of infected bread, by administering large quantities of coffee, and by applying warmth and friction to the affected extremities. When gangrene actually occurs, expectant treatment should be adopted, surgical interference being deferred until a definite line of demarcation has formed.

II. GANGRENE DUE TO DEFECTIVE INNERVATION

Disorders of the nervous system predispose to, or actually cause, gangrene, without any coexisting vascular disease, as is clearly demonstrated by Raynaud's gangrene, anæsthetic leprosy, and the occurrence of sloughing on the paralysed side in cases of hemiplegia, even though the patient has been laid upon the unaffected side and every precaution has been taken to prevent pressure and microbic infection. But undoubtedly, in the majority of cases, defective *innervation only acts as a predisposing cause of gangrene by modifying the nutrition of the part*, and interfering with the defensive properties of the tissues against bacterial infection, thereby allowing pressure, or thermal and chemical agents, to act as the exciting cause

myelia, and certain forms of neuritis. When occurring as a pathological entity, the condition is not a serious one, and seldom leads to more than superficial necrosis. It is generally seen in women between the ages of 18 and 30, is often developed by cold, affects the fingers of one or both hands, and less commonly the toes, the tips of the ears, and the nose. The term "Raynaud's gangrene" should only be applied to those cases which are preceded by certain phenomena known as local syncope and local asphyxia, and which are unaccompanied by obstruction or disease of the main arteries.

Symptoms.—Very often, as the result of some mental shock, or under the stress of intense emotion, the fingers become pale, bloodless, insensitive, and shrunken, owing to contraction of the arterioles (*local syncope*). In time the spasm is followed by relaxation, and the digit becomes warm, hyperæsthetic, and, owing to the extremely sluggish circulation, so deeply congested as to be almost black (*local asphyxia*). These attacks occur more often in the winter, and, apart from hysterical manifestations, may start during or after a meal, when getting up in the morning, or when the patient is tired. If recovery is incomplete between the paroxysms the duskiness of the fingers continues for some days, the pain increases, small sanious blebs form, and at first sight it appears as if several fingers were about to die. Ultimately, however, the circulation gradually improves, the normal colour returns, and only a small area of skin and subcutaneous tissue becomes gangrenous and is cast off as a dry, black slough. The whole process is so slow that weeks or months may elapse before separation is accomplished. The condition occasionally simulates senile gangrene and so may give rise to difficulties in diagnosis, but if it be remembered that Raynaud's disease is generally bilateral, is limited to the skin and subcutaneous tissues, affects several digits, attacks the fingers more often than the toes, and is unassociated with arterial disease, a mistake is not likely to occur.

Treatment.—When gangrene is threatened, local treatment consists in soaking the fingers in tepid salt water, drying them thoroughly, and wrapping them up in cotton-wool or thick woollen gloves. Necrotic patches must be enveloped in dry aseptic dressings and allowed to separate naturally. General constitutional treatment should be directed against the disease, and opium may be given in small doses for the relief of pain. Cases of Raynaud's disease affecting the hands alone have been recorded in which the symptoms have been ameliorated by stretching the median and ulnar nerves; but this line of treatment is, of course, only suitable when the disease is independent of an organic lesion. (*See also* the conservative treatment of senile gangrene, p. 250.)

Gangrene due to ergot.—The prolonged ingestion of bread made from rye infected with the *Claviceps purpurea* leads to tonic contraction of the peripheral arterioles, degeneration of their inner coats, thrombosis, and dry gangrene. Ergotism is now very rare, and practically limited to Central and Eastern Europe. It is liable to occur in cold wet summers (climatic conditions that favour the growth of the fungus), and mainly affects the poorer agricultural classes, who are often obliged to live on bread made of the diseased grain that cannot be sold. Middle-aged men appear to be peculiarly susceptible to the poison, and develop gangrene more often than women and children, owing to premature arterio-sclerosis from hard work or chronic alcoholism.

Symptoms.—The early signs of ergotism are manifested by disturbances of the central nervous and digestive systems. Giddiness, buzzing in the ears, blurred vision, numbness, tingling, and hyperæsthesia are accompanied by attacks of diarrhœa and vomiting; later, spasm of the muscular arterioles causes painful burning cramps, defective circulation, and coldness of the extremities At this stage gangrene due to peripheral thrombosis is very apt to occur. It is usually of the dry type, often bilateral, generally affects the toes and feet, although the fingers, nose, and ears may be attacked. The process is so slow that one or two years may elapse before the dead part separates, while the amount lost varies from a digit to the greater portion of an extremity.

Treatment.—The premonitory symptoms, if recognized, may be relieved and the gangrene prevented by cutting off the supply of infected bread, by administering large quantities of coffee, and by applying warmth and friction to the affected extremities. When gangrene actually occurs, expectant treatment should be adopted, surgical interference being deferred until a definite line of demarcation has formed

II. GANGRENE DUE TO DEFECTIVE INNERVATION

Disorders of the nervous system predispose to, or actually cause, gangrene, without any coexisting vascular disease, as is clearly demonstrated by Raynaud's gangrene, anæsthetic leprosy, and the occurrence of sloughing on the paralysed side in cases of hemiplegia, even though the patient has been laid upon the unaffected side and every precaution has been taken to prevent pressure and microbic infection. But undoubtedly, in the majority of cases, defective innervation only acts as a predisposing cause of gangrene by modifying the nutrition of the part, and interfering with the defensive properties of the tissues against bacterial infection, thereby allowing pressure, or thermal and chemical agents, to act as the exciting cause

Well-known examples of this type are the bed-sores and splint-sores that form on paralysed parts as the result of continued pressure, the perforating ulcer of the foot that develops (again as the result of pressure) in tabes dorsalis, and the painless whitlows and extensive burns that occur in syringo-myelia. Except Raynaud's disease and anæsthetic leprosy, the form of gangrene that occurs in these cases is always moist, generally septic, and spreads rapidly if extension once begins.

Treatment.—A paralysed limb should always be kept warm, and all sources of pressure avoided or removed. Should sloughing occur, it must be treated like a bed-sore (p. 247). If spreading moist gangrene affects an extremity, an amputation well above its limit is clearly indicated

III. GANGRENE DUE TO INJURY (DIRECT TRAUMATIC GANGRENE)

The term "direct traumatic gangrene" is employed to denote death of the tissues from a severe injury when the necrotic process takes place at the point of application of the violence. For instance, the passage of a cart-wheel over the fingers or toes will so lacerate the vessels and crush the tissues that their vitality is destroyed at once. Injuries of this kind, if applied at a higher level, will not only cause direct gangrene, but, by damaging the vessels and nerves leading to the lower part of the limb, may also lead to indirect gangrene of distal parts, as has been described in the section devoted to gangrene following injuries of vessels.

Symptoms.—Direct traumatic gangrene is always primarily moist, because the injured tissues are loaded with fluid at the time of death; but the local appearance and constitutional symptoms will depend upon the possibility of securing asepsis immediately after the injury. If all efforts in this direction fail, the typical signs of septic moist gangrene will develop and spread with rapidity, while the patient suffers from severe constitutional symptoms due to absorption of the products of putrefaction. But if the case is seen early, and efficient measures are taken to ensure asepsis, local signs and constitutional symptoms of septic moist gangrene do not appear. The dead part either separates *en masse* by a process of aseptic moist gangrene, or it becomes infiltrated with connective-tissue cells, which, together with the leucocytes in the effused blood, gradually remove the necrotic material and form fresh tissue. This latter process is identical with that known as healing by blood-clot. While this is taking place, though a small portion of the dead tissue may separate in the form of a dry slough, the zone of inflammatory reaction is very slight, and consti-

tutional symptoms are conspicuous by their absence. Lastly, if at the time of injury the lacerated tissues are infected with dust and dirt in which various gas-forming bacilli are present, one of the most serious forms of gangrene—viz. gas gangrene—will appear and spread with fearful rapidity. Owing to the method of its production, this latter variety is sometimes called acute spreading traumatic gangrene.

Treatment.—From the foregoing it will be readily understood that the keynote to success is the promotion of asepsis. Of course, when a foot or a hand is crushed to pulp, or when a comminuted fracture makes it exceedingly unlikely that the limb will be of any use, the only possible procedure is an immediate amputation through living tissues; but, when the part is not quite so severely injured, it may be possible to save it by adopting conservative measures. For this purpose a general anæsthetic is advisable, in order that the extent of the injuries may be ascertained and the wound thoroughly cleansed. After hæmorrhage has been arrested and foreign bodies, loose pieces of tissue, bone, etc., have been removed, the edges of the lacerated skin and injured tissues should be excised *en bloc*. The wound is then treated by the Carrel-Dakin method until all danger of gangrene has passed.

In the event of limited gangrene setting in, conservative treatment is only permissible when it is judged that a useful limb will be obtained after the separation of the dead part. If this appears impossible from the nature of the injury, or if the patient is old and debilitated, or if the gangrene, though limited, is accompanied by septic intoxication, early amputation is called for.

IV. GANGRENE DUE TO PHYSICAL AND CHEMICAL AGENTS

1. Gangrene due to heat.—As burns and scalds are described in a separate article (p. 309), it is sufficient to point out here that heat causes gangrene by inducing coagulation of the albuminous elements of the tissues. A temperature of 132° F. coagulates myosinogen and fibrinogen, and therefore solidifies and destroys the tissues.

2. Gangrene due to cold.—The ultimate effect on the body of a low temperature is determined by the degree of cold, the period of exposure, and the resistance of the tissues. Damp cold, owing to the obstacles it raises to efficient evaporation, produces more serious results than dry cold. Short exposure to intense cold, or prolonged exposure to a less severe degree of cold, may result in nothing more serious than a chilblain; but prolonged exposure to intense cold, particularly in those who are weakly or debilitated

either by age or alcohol, causes frost-bite or, in other words, gangrene. The first effect of cold is to cause contraction of the blood-vessels and, in consequence, slowing of the circulation and blueness of the skin. If exposure is prolonged, the vessels contract to such an extent that the circulation ceases altogether and the skin becomes white and insensitive. If this condition is allowed to exist for any length of time, necrosis takes place from anæmia; or if warmth is suddenly applied to the part, which, though pale, still retains its vitality, vaso-dilatation is so excessive that stasis and thrombosis occur, and the tissues, already enfeebled by defective circulation, become gangrenous. As might be expected, the parts most often affected are those most exposed—the fingers, toes, ears, and nose.

Symptoms.—The local effects of cold are manifested in several ways. A limited exposure to intense cold renders the skin œdematous, swollen, and dusky-red. The redness disappears on pressure and returns very slowly. This condition is known as *pernio* or *chilblain*, and the phenomena which accompany it are due to the sluggish circulation. The patient's attention is attracted by the sensation of burning and intolerable itching that exposure to heat induces. The toes and fingers are usually attacked; and the condition tends to disappear as the warm weather approaches. Should the cold act for a longer period, obstinate cracks and fissures appear, or a blister may form and be followed by an acute spreading ulcer which is atonic and very slow in healing. When gangrene develops the skin becomes livid and marbled, bullæ form rapidly, and the necrotic tissue separates in the form of dry white or black sloughs.

In some instances the reactionary inflammation and its attendant thrombosis may be so extensive as to lead to the death of a whole limb. In these cases the gangrene has a great tendency to become dry, spreads very slowly, and, as in senile gangrene, may repeatedly extend beyond an abortive line of demarcation

Treatment.—A patient affected by cold, and threatened with frost-bite, should be removed from the low temperature as soon as possible and placed in a room with a very small fire, for if he be brought immediately into a warm atmosphere, sudden vaso-dilatation and thrombosis will be favoured The threatened parts should never be rubbed with snow or other gritty and possibly defiled material. Very gradual thawing is to be obtained by applying an ungloved hand to the part threatened; in cold climates the bare hand soon cools and a too rapid thawing is avoided Later it may be replaced by the other hand, which has hitherto been kept gloved. The temperature of the room may then be gradually raised to 60° F., at which it should be kept until the vitality of the part is assured. After the thawing the parts should be dressed with a paraffin-lano-

lin-eucalyptus preparation that is flexible at body temperature. The patient should then be wrapped in blankets, put to bed, and given lukewarm soup or coffee, but no alcohol. If gangrene supervenes, the part must be kept dry and aseptic while a line of demarcation is awaited A superficial slough, or a small portion of a digit, may be left to separate naturally, but gangrene of a portion of an extremity should be treated by amputation at a convenient distance above its limits when a permanent line of demarcation appears.

3. **Gangrene due to escharotics.**—*Strong acids* and alkalis cause immediate local necrosis by their caustic action. Acids coagulate the blood and cytoplasm, while alkalis cause liquefaction of the tissues; hence in the former the gangrene is dry, and in the latter moist. Within recent years many cases of gangrene due to the local application of *carbolic acid* have been recorded. In nearly every instance it followed the employment of a dilute solution (1 : 100, 1 : 50), applied for several hours as a wet dressing to a finger or toe. The death of the part is due to a direct chemical action on all the tissues, for the epidermis, by first becoming œdematous, loosened, and devitalized, allows the watery solution of the acid to soak into and destroy the deeper layers, its action in this respect being analogous to that of mineral acids. Different observers have proved that carbolic-acid gangrene may be produced in twenty-four hours by a 1-per-cent. solution, in twelve hours by a 2-per-cent. solution, and in three or four hours by stronger solutions.

Symptoms.—Following the application of a carbolic-acid compress, blanching and crenation of the skin are accompanied by itching and paræsthesia gradually merging into anæsthesia. The loss of sensation is comforting to the patient, particularly if the compress has been applied to a painful finger, and induces him to leave the dressing undisturbed. When it is eventually removed, the digit is found to be stiff, cold, insensitive, and pale-yellow or brown.

Treatment.—The choice lies between amputation and awaiting the formation of a line of demarcation with natural separation. Of these, the former is preferable, as soon as the inflammatory reaction has subsided.

V. GANGRENE DUE TO INFECTIVE PROCESSES

There are four varieties of gangrene that fall under the above heading: those due (1) to *acute inflammation*, (2) to *gas gangrene*, (3) to *cancrum oris*, and (4) to *phagedæna*. In these forms the death of the tissues is primarily caused either (*a*) by the more or less mechanical effect of an acute inflammation excited by the presence of bacteria, or (*b*) by the direct devitalizing action of toxins

The distinction here indicated is a very important one, both from the pathological and from the clinical standpoint, inasmuch as the part that bacteria play has a very definite bearing on the symptoms and treatment. In that form of gangrene brought about by acute inflammation, the immediate constitutional symptoms are not always severe, and the process may often be limited by a timely incision which has for its object the restoration of the circulation by relieving the pressure exerted by an excessive exudate; but in that variety in which necrosis is due to the direct action of bacterial toxins, death of the tissues is so rapid that an inflammatory barrier has little or no time to form, consequently the gangrene spreads with alarming rapidity, is accompanied by the gravest constitutional symptoms, and nothing short of immediate and wide removal of the affected part will suffice to save the patient's life. From the foregoing it will be readily understood that all the forms of gangrene due to infective processes are of necessity moist.

1. **Gangrene due to acute inflammation.**—This form is particularly prone to follow acute inflammation when it occurs in dense tissues, and is typified by boils, carbuncles in the skin, and necrosis of bone. Its mode of production is similar in each instance. Bacterial action causes such an intense inflammation that the circulation through the part ceases, either owing to the occurrence of extensive stasis or as the result of pressure on the vessels by excessive exudation. When bone is attacked necrosis takes place with great rapidity, for its vessels, being contained in rigid canals, are soon compressed by the exudate, and, if the periosteum is also stripped up by the formation of pus beneath it, the only remaining source of blood supply is cut off. Thus a large portion of bone may become entirely deprived of its circulation and die. Circumscribed inflammation in the superficial layers of the skin produces a similar result, manifested by the small core of a boil or the large slough of a carbuncle. That the formation of the slough is due solely to the density of the tissues in which the inflammation commences, and not to the action of bacterial toxins, is sufficiently proved by the occurrence of abscesses instead of boils in the flaccid skin of the scrotum, or in the thin skin of children.

2. **Gas gangrene (acute spreading traumatic gangrene).**—In civil practice this is a comparatively rare disease and used to be designated emphysematous gangrene, but during the Great War, when it occurred with appalling frequency in the early years, before the proper method of treating recent wounds was understood, it became known as gas gangrene. What is here described is gas gangrene as seen during the War, though with certain modifications it may be applied to the milder varieties met with in civil life.

It must be clearly differentiated from that great class of moist gangrene in which gas-formation is due to the putrefactive changes that take place in tissues already dead or dying from some other cause; for in gas gangrene bacterial infection leads to gas-formation and primary gangrene, often without preceding inflammation, while in the other form bacterial infection is a secondary process.

Etiology.—The disease is due to the inoculation of lacerated tissues (especially muscles) with anaerobic gas-producing micro-organisms. On certain clinical and bacteriological grounds (*see* later), the disease is regarded by many as essentially one of muscles, but laboratory workers do not agree with this hypothesis, for they have produced the identical disease in an animal by subcutaneous injection of anaerobic organisms. Though one or more varieties of the specific organisms are found in every case of gas gangrene, their presence in the tissues does not necessarily imply that gangrene will develop, for during the War they were often found in wounds, both recent and old, and in collections of blood (e.g. hæmothorax), in which there was no sign of gangrene and only a trace of gas infection.

As the specific organisms are intestinal in origin, they are always implanted in wounds which have been contaminated with manured soil, pieces of dirty clothing, or fæcal matter. Clinically, this is shown by the fact that the mortality from gas gangrene of wounds of the lower limb, therefore nearer the soil, was far greater than of wounds of the upper limb, and that gas gangrene was practically unknown in desert and mountainous regions.

Conditions favouring the occurrence of gangrene.—(1) Extensive laceration and crushing of the tissues by shell and bullet wounds, street accidents, etc., especially when complicated by large extravasations of blood, and by fracture and comminution of bones. As the anaerobes causing gas gangrene are mostly saprophytes, partially devitalized or dead tissues form the best medium for their growth.

(2) Interference with the circulation, by division or occlusion of the main artery to the part, or by the pressure of a tourniquet or tight bandage. This is the commonest cause of "massive" or "group" gangrene in which groups of muscles in a limb become gangrenous and infiltrated with organisms from end to end. Also, as Taylor and Wallace have pointed out, loss of blood supply of lesser degree accounts for the presence of a gangrenous muscle in the midst of a healthy group, and for gangrene of part of a muscle with a double blood supply when only one vessel is injured.

(3) Retention of extravasated blood and discharges by a tight plug, a hard dried dressing, or imperfect drainage of a wound.

(4) Buried missiles, foreign bodies, portions of clothing, etc.

(5) Low blood-pressure from hæmorrhage, cold, and shock.

(6) Lowered vitality from constitutional disease or any other cause For example, a man who has been previously "*gassed*" is more liable to develop gas gangrene from a trivial wound.

Bacteriology and biochemistry of gas gangrene.—At least ten different organisms have been isolated from cases of gas gangrene. All of them are fæcal in origin, and the majority are anaerobic spore-bearers, giving vigorous fermentation reactions in the presence of organic material. Herbert Henry has divided them into two main groups, according to their biochemical activities—the saccharolytic and the proteolytic.

The *saccharolytic* group contains—

(1) *B welchii* (synonyms, *B aerogenes capsulatus* of Welch and Nuttall, *B. perfringens* of Veillon and Zuber, *B. phlegmonis emphysematosæ* of Fraenkel).
(2) *B. tertius* (synonyms, *Bacillus Y* of Fleming, *B. von Hibler IX* or *B. rodella III* of Robertson).
(3) *B. fallax* of Weinberg.
(4) *B aerofœtidus* of Weinberg.
(5) *B. œdematiens* of Weinberg.
(6) *Vibrion septique* of Pasteur (synonym, *B. œdematis maligni* of Koch).

All these organisms can be differentiated by their sugar reactions. Though some of them are also proteolytic, their activities in this direction are slight in comparison with those of the next group.

The *proteolytic* group includes—

(1) *B. sporogenes* of Metchnikoff.
(2) *B. histolyticus* of Weinberg.
(3) *B. putrificus coli* of Bienstock.
(4) *B. cadaveris sporogenes* of Klein.
(5) *B. tetani* of Nikolaier.

These organisms are mainly proteolytic, and though they all ferment dextrose, lævulose, and maltose, their saccharolytic power is comparatively slight.

Though the infection is usually a mixed one, due to *B. welchii* and *B. sporogenes*, it may be caused, in the order of frequency and importance, by either *B welchii*, *Vibrion septique*, *B. œdematiens*, or *B. fallax* alone.

B. welchii produces the greatest quantity of gas, a yellow *œdema*, and brick-red muscle ("red death").

B. œdematiens appears to be associated with a specially severe form of gangrene, characterized by acute general intoxication, extensive spreading, and solid œdema, with little gas-formation. The dead muscles are pale pink in colour.

B. sporogenes gives rise to the characteristic fetid odour of the wound and discharges. The muscles are diffluent and green or black.

The *anaerobes* usually remain localized to the tissues, but in serious cases, immediately before death, they may be found in the blood-stream. Rare cases of metastatic gangrene, in which gangrene suddenly appears in another part of the body subjected to pressure, such as the buttock, or at the site of puncture by a hypodermic or infusion needle, can only be accounted for by hæmic infection. *Aerobes*, such as *non-hæmolytic cocci, enterococci*, and *streptococci*, may be found in combination with the anaerobes. One of these, *Streptococcus fæcalis*, commonly found in manured soils, is therefore part of the primary infection, but *Streptococcus pyogenes* is only found in a small percentage of recent wounds, and probably plays no part in the incidence of gas gangrene.

Perhaps the most lucid account of the changes produced by anaerobes in the tissues is given by Herbert Henry (*British Medical Journal*, June, 1917, p. 806), whose article is therefore freely used. He states that in a wound the members of the carbohydrate-splitting group of anaerobes are the first to develop. The glycogen which is found in living healthy muscle is rapidly converted after death into dextrose and a small fraction of isomaltose. Both these substances are vigorously fermented by *B welchii*, and it is because of their presence that this organism so readily establishes itself in damaged muscle. This early fermentation results in the formation of acid and gas. The latter consists of a mixture of CO_2 and hydrogen, which develops with astonishing rapidity. Coincident with the production of gas is the formation of various organic bodies. The acids inhibit the growth of the organisms, but if they are neutralized by a salt, such as calcium or magnesium carbonate, the growth becomes more luxuriant and its vitality increases. In infected tissues, such neutralization is brought about by the inflammatory exudate and, in all probability, by the presence of soluble calcium salts in the soil with which the wound is infected Another factor which comes into play is the growth of organisms of the proteolytic group, e.g. *B. sporogenes*, which attack the proteins of the damaged tissues, finally leading to the production of ammonia bodies, which in turn neutralize the acids resulting from carbohydrate fermentation. The gas formed by the proteolytic organisms owes its foul smell to the presence of sulphuretted hydrogen and volatile bodies. It is thought that the chemistry of the soil plays an important part in gas gangrene, particularly in fulminating cases which occur within a few hours of an injury, for the incidence of the disease is more frequent in areas where the soil is rich in soluble calcium salts. Experimentally, it has been proved that when a washed and detoxicated culture of *B. welchii*

is injected *subcutaneously*, and not intramuscularly, together with small doses of calcium chloride, an animal will die in twenty-four hours of fulminating gas gangrene. Post-mortem examination shows bacilli distributed throughout the body, but reveals no special predilection for muscle. The probable explanation is that, given a suitable pabulum in the form of devitalized tissues, particularly muscle, anaerobic organisms, which in ordinary circumstances are not pathogenic, will grow and form toxins which the tissues are unable to neutralize, and that the process is greatly assisted by, if not actually dependent on, the presence of soluble calcium salts, carried in with the soil at the time of injury. This also explains the incidence of the milder forms of gaseous cellulitis and gas gangrene in civil life, in which the muscles are not necessarily injured, though infection is due to identical organisms. In these cases the soil infecting the wound probably contains sufficient soluble calcium salts to enable the anaerobes to overcome the tissue resistance, whereas in a gunshot wound there is, in addition, enough devitalized or necrotic muscle to form the most favourable medium for their growth and toxin-production. When it became known that the toxin produced by *B. welchii* or the *Vibrion septique* was about a thousand times less powerful than tetanus toxin, it was difficult to account for death from gas gangrene in so short a time as eighteen hours, when death from tetanus seldom occurs before the second day. The greater multiplication of pathogenetic bacteria, and consequent greater formation of toxin in gas gangrene, fail to explain the rapid toxæmia. Bulloch and Cramer consider that the explanation lies in the constant changes found in the suprarenal bodies of animals killed by *B. welchii* or *Vibrion septique*, changes which have also been found in actual cases of gas gangrene in man. Apart from certain cortical lesions, the important change in the gland is the complete disappearance of adrenalin from the medulla. Experimentally, it has been proved that, in the absence of adrenalin, non-lethal doses of toxin become lethal.

From the foregoing, it will be understood that the chemistry of anaerobic growth, toxin-formation, and subsequent destruction of the host is a very complicated process and depends upon the establishment of a vicious circle which may be thus briefly outlined: *B. welchii* (saccharolytic) → carbohydrate fermentation → gas + acids → inhibition of *B. welchii* by acids → *B. sporogenes* (proteolytic) → [illegible] of adrenals → toxæmia.

Pathology.—The inoculation of a wound with *B. welchii* is immediately followed by an enormous migration of leucocytes, which ingest and destroy the bacilli in great numbers. When bacterial growth



Fig. 1



Fig. 2.



Fig. 3



Fig. 4

Colour changes in gas gangrene.

Fig. 1.—Normal colour of gluteus maximus, from a patient who died of acute peritonitis.

Fig. 2.—Dead muscle, non-contractile, crepitant to the touch, and brick-red in colour. Spaces once occupied by gas-bubbles can be seen.

Fig. 3.—Muscle at a further stage, colour passing from brick-red to olive-green.

Fig. 4.—Terminal stage, muscle greenish-black, soft and diffluent.

(After Sir Cuthbert Wallace, by permission of the British Medical Journal and H.M. Stationery Office

overtakes leucocytosis, the toxin formed inhibits emigration and kills the leucocytes, with the result that the bacilli increase with enormous rapidity, invade fresh, healthy tissues, and the gangrene spreads. When cellular tissue alone is involved, as in some cases seen in civil life, this process is not necessarily very rapid or serious, but when the bacilli are implanted in muscles already devitalized by a serious injury, or by a defective blood-supply, they are provided with the best pabulum for their growth and toxin-formation. A large hæmorrhage into a fascial compartment has a similar effect by causing pressure anæmia, and finally the toxin assists bacillary growth by causing thrombosis when it reaches a vein. When once the disease has established itself, dissemination takes place by direct extension in muscles, in loose connective tissue, along lymphatics, and by invasion of the blood-stream.

The most characteristic lesions of gas gangrene are gas-formation and necrosis. The gas develops with astonishing rapidity, and may be clinically evident as early as three hours after the receipt of a wound. In the early stages it is odourless and can be ignited with a lighted match, but later it becomes malodorous, owing to the formation of sulphuretted hydrogen and other products of decomposition. If muscles are injured, it is formed first in them, and later reaches the cellular tissue by escaping through holes in the fascia, or by the side of the perforating arteries and nerves The muscles lose their striation and pass through the various changes leading to coagulation necrosis (Plate 28). They crepitate with the gas bubbles which form between their fibres, they no longer contract when stimulated, and their colour changes to a dirty brick-red ("red death") Next they become friable and yellow, and finally, when proteolytic digestion is established, the dead muscle becomes soft, diffluent, and eventually black from the action of sulphuretted hydrogen on the iron liberated from broken-down hæmoglobin In muscle the disease is a longitudinal one, and may be limited to one muscle, and even to an anæmic portion of that muscle. The organisms tend to remain within the limits of the epimysium; when they spread to neighbouring muscles they do so by way of the subcutaneous tissue or the deep connective-tissue trabeculæ. Two of the most striking effects are the entire absence of any inflammatory reaction, and the presence of a dead muscle, crackling with gas, in the midst of a group of perfectly normal, healthy, contractile muscles. In this connexion it is worthy of note that all injured muscles are not equally liable to infection. The glutei appear to be particularly susceptible, possibly owing to the proximity of the wound to the anus, while the muscles of the back, neck, and scalp are seldom affected.

The walls of the blood-vessels undergo necrosis together with the

other tissues, and thrombosis is common in the veins and capillaries, thereby aiding the extension of gangrene. When the fibrous sheaths of the nerves are destroyed, the myelin sheaths of the axis-cylinders undergo the changes which characterize degeneration. Lesions in the other organs are due to the circulation of toxins and bacteria. Hæmolysis is fairly constant and occurs early. In the liver, areas of necrosis and gas bubbles surrounding colonies of bacilli may be found. Similar changes occur in the spleen, but even here, as in the liver, there is never any cellular exudate. The changes in the kidney are constant and severe and are characterized by cloudy swelling and disintegration of the epithelial cells. While these changes are taking place locally, the chemical products of decomposition are formed in great profusion; liquefaction proceeds so rapidly that dressings become saturated with fluid, bubbles of foul-smelling gas quickly spread along the planes of loose connective tissue, and the part becomes converted into a slimy, crepitating mass with a penetrating, fetid odour.

X-ray appearances in gas gangrene.—A radiogram, when positive, may be of great value in revealing the presence of gas, its extent and situation (Plate 29), but no reliance can be placed on a negative result. As gas bubbles will only show on a plate when present in fair quantity, this aid to diagnosis is of most use in cases of delayed gas gangrene occurring some days after an injury, and in localized anaerobic infection of a wound. In the latter instance especially, a positive radiogram will indicate the necessity for a more thorough operation than might otherwise have been thought necessary. Also, when amputation is required for gas gangrene with typical clinical signs, a radiogram may show the extent of tissue involved.

Briefly, the appearances and deductions are as follows: (1) Fine striation of individual muscles = *Vibrion septique*. (2) Simple swelling with a pale, misty outline = *B. welchii*. (3) Shadows like dark, woolly clouds, with occasional sharply outlined bubbles = *B. welchii* and *B. sporogenes* together.

Fallacious shadows are thrown by extensive ecchymosis, small hæmatomas, abscesses, and actual loss of tissue.

Varieties of the disease.—Gas gangrene may be—

(1) A localized anaerobic infection.

(2) "Group" gangrene (gangrene of a single muscle or of a group of muscles).

(3) Segmental or "massive" gangrene (gangrene of a whole segment of a limb).

(4) Fulminating gangrene.



Gas gangrene of knee-joint and leg, showing striation of gas-bubbles with separation of muscle-fibres.

(Frances Ivens, M.B., M.S., "Proc. Roy. Soc. Med.")

PLATE 29.

Symptoms.—The time which elapses between the injury and the onset of gas gangrene varies within wide limits. The gangrene may begin within two hours of the infliction of the wound, or be delayed for many weeks. A characteristic feature is the dramatic suddenness with which the disease begins: a patient left in good condition overnight may be found acutely ill and on the verge of death in the morning. Early symptoms are pain, due to the accumulation of gas under pressure, numbness in the superficial parts of the limb, restlessness, and malaise. Vomiting is common from the outset, and may become very severe in the later stages. Constitutional symptoms soon make their appearance. Depression becomes extreme; the patient looks very ill, with a dry, brown tongue, great thirst, and a pale, sunken expression. Later, the pallor, which is so marked as to give the impression that there is, or has been, a severe hæmorrhage, changes to a muddy colour, and towards the end there may be generalized icterus. The pulse increases, and finally becomes soft, running, and altogether uncountable. The temperature may rise several degrees at the onset of the disease, but falls suddenly as the patient becomes more toxic, and thus indicates a fatal termination. In the terminal stages sweating is profuse, the lips are cyanosed, and the extremities cold and blue. One of the most distressing features of the disease is the mental clarity which persists to the very end. Death takes place with extraordinary suddenness: a patient may die peacefully in his sleep, or suddenly, when sitting up in bed, carrying on a perfectly rational conversation

Physical signs and treatment.—(1) With a LOCALIZED ANAEROBIC INFECTION, the only distinctive sign is a copious, watery, rust-coloured, malodorous discharge composed of disintegrated blood-clot and bubbles of gas. The skin around the wound, at first white, soon turns red or purple, and as the disease progresses the surrounding parts become swollen and crepitant with gas

Treatment.—The affected skin, fascia, and any underlying devitalized tissues should be removed *en bloc* as soon as possible There should be no hesitation in making incisions long enough to give free access to all infected structures. Embedded foreign bodies, pieces of clothing, etc, should be searched for and removed at the same time. The large wound—and it is important that the wound should be large—must be left wide open, lightly packed with sterile gauze in which Carrel tubes are embedded, and irrigated with Dakin's solution every two hours. Any infected parts, such as bone, large arteries, or nerves, which cannot be excised, must be cleaned as well as possible by gauze swabs soaked in an antiseptic. Secondary suture *can* be performed when a healthy granulating surface has been obtained.

(2) "GROUP" GANGRENE (Plate 30).—In the early stages the limb

may appear normal, or it may be more or less swollen. The skin may also *be normal, or tense and blanched from* the underlying swelling. The area around the wound, or even the whole limb, soon becomes *crepitant and tympanitic.* As the disease progresses, the swelling increases, crepitation spreads rapidly, and the skin becomes mottled, then purple, and finally greenish-yellow. These colour changes are accompanied by the formation of blebs and bullæ containing foul-smelling, sanious fluid. In some instances the skin becomes bronzed, but the exact cause of this is unknown. According to Wallace, this discoloration is not common on the limbs, but is more often seen on the body in connexion with wounds of the extraperitoneal part of the colon. Its appearance may have no particular significance, or it may be followed by extensive sloughing of the skin and death of the patient.

While these changes *are taking place in the skin, quantities of* yellow fluid, due to hæmolysis, with a peculiarly disgusting odour, *pour from the wound* in such quantities as to soak and *stain the* dressings. It should be realized that the colour of the skin is not an absolute indication of the condition of the subjacent *tissues. A* purple hue signifies dead and gangrenous muscle, but, conversely, gangrenous muscles may underlie normal skin. The muscles, if exposed, are swollen with exudate and gas, they do not contract on stimulation nor bleed when incised, and undergo characteristic changes in colour, being first dry and brown, then brick-red, and finally black or green and pultaceous.

Treatment.—This varies with the general condition of the patient.

(A) *Patient in good condition.*—The mechanical cleansing of the wound is proceeded with as already indicated. All affected tissues are exposed by adequate longitudinal incisions. The colour and condition of the muscles are noted, care being taken to exercise the greatest gentleness, otherwise the blood supply to a healthy muscle may be damaged, and in consequence it may die and become infected. All muscles which do not contract or bleed, or are altered in colour, are excised. Certain muscles may require total excision; in others, removal of a portion may suffice. Attention to these details *may result* in the preservation of a limb which from the extent of crepitation present would otherwise have been amputated. Crepitant *subcutaneous* tissue should be freely incised and, as in the preceding case, the whole wound should be treated by the Carrel-Dakin method.

(B) *Patient in bad condition.*—This occurs most often in connexion with a fracture of one of the long bones, and is best *treated by amputation* at the site of fracture. When swelling and crepitation suggest the necessity for amputation at a higher level than *the fracture, it is advisable to ascertain the condition* of the tissues at the



Amputated arm, showing colour changes in gas gangrene ("group" type)

Note purple mottling of skin, and contrast between infected flexor muscles seen through wound, and normal-coloured muscle by side of divided humerus.

(After Sir Cuthbert Wallace, by permission of the British Medical Journal and H M. Stationery Office)

PLATE 30

proposed level by longitudinal incisions, before proceeding with the higher amputation. Occasionally, it is possible to amputate at the site of fracture and to excise a single dead muscle, such as the sartorius or biceps, through an adequate longitudinal incision. Whenever possible, it is advisable to fashion short skin-flaps; these are turned back until all danger of further infection is over, when they can be pulled down and made to cover the stump by the application of strapping and weight-extension. The best form of amputation for gangrene of the *leg* is by the guillotine method through the head of the tibia or through the knee-joint, with excision of the condylar attachments of the gastrocnemius. The raw surface must be treated by the Carrel-Dakin method and closed by secondary suture, or re-amputated at a higher level when all danger of further infection has passed.

(3) "MASSIVE" or SEGMENTAL GANGRENE follows injury of the main artery of a limb. There are two types of the disease. In one, sudden crepitation in a limb already dead from loss of its blood supply is followed by the typical constitutional symptoms of gas gangrene; in the other, necrosis, gas-infection and constitutional symptoms appear simultaneously. In both varieties the appearance of the skin at the outset is that of ordinary arterial gangrene, but the subsequent stages of discoloration follow each other more rapidly than in the "group" type.

Treatment.—Gangrene may be prevented, or its extent lessened, if an adequate flow of blood can be maintained either by suture of the injured artery, or by the use of a Tuffier's tube until the collateral circulation has developed. When gangrene has occurred, amputation should be performed at the lowest level of living muscle, but if there is a concomitant severe injury of a bone or joint above the gangrene the amputation should be performed at a higher level

(4) The FULMINATING TYPE spreads with fearful rapidity and quickly proves fatal. It owes its virulence either to a very severe infection, or to the patient's lowered resistance. It usually takes the form of the "group" or "massive" type, in which the changes occur so rapidly that they can be followed from hour to hour, but occasionally it occurs as an odourless, rapidly spreading, gelatinous white œdema. In both forms the pain and swelling are excessive and the constitutional symptoms severe.

Treatment.—This variety of gangrene is practically always fatal, and, when a limb is affected, the patient's only hope lies in rapid amputation as high as possible. Should the divided tissues be already infected, they must be laid open by free incisions and irrigated continuously by the Carrel-Dakin method. When the disease occurs in a recent amputation stump, surgical measures are generally useless.

Preventive treatment.—This paragraph has been placed purposely at the end of the section in the hope that the reader will have appreciated the factors which predispose to gas gangrene, and will therefore be in a better position to remember the following important points:

(1) As a defective blood supply favours anaerobic infection, particular care must be taken to avoid the pressure of a tourniquet, tight bandages, or unsuitable and improperly applied splints.

(2) Dressings must be kept continuously moist, as when dry they soon become hard and prevent the escape of discharges, which in turn impede the circulation and also aid bacterial growth.

(3) For the same reason, the use of tight plugs and antiseptic pastes in a recent wound is contra-indicated.

(4) A fractured long bone should be temporarily fixed as soon as possible on some form of splint with an extension, owing to the danger of a displaced fragment pressing on the main artery of the limb.

(5) Severe shock or hæmorrhage must be treated by appropriate measures, such as warmth, morphia, gum saline, or blood infusion.

(6) Last, but by no means least, the surgical treatment and mechanical cleansing of the wound must be carried out as soon as possible. All dressings and swabs soiled by discharges must be burnt, and the instruments used during the operation boiled in carbolic lotion (1:20) for one hour, in order to destroy the anaerobes and their spores.

General treatment consists in the administration of stimulants and of anodynes when necessary. As there is always some degree of acidosis, an intravenous infusion of a 4-per-cent. solution of sodium bicarbonate is beneficial, and often has a remarkable effect in improving the colour and general condition of the patient.

Antitoxic serums were used both prophylactically and therapeutically during the War, but the benefits derived from them were not sufficiently noticeable to justify any great enthusiasm. The difficulties lie in the mixed character of the infection, in the recognition of the predominant organism, and in the administration of the appropriate serums in suitable proportions The results of much experimental work have shown that serum should be given at the earliest possible stage in the illness, and that it should contain antitoxin to *B. welchii, Vibrion septique, B. œdematiens*, and *B. fallax*.

3. **Cancrum oris** and **noma vulvæ** are the names given to a destructive, and often fatal, form of gangrene which attacks the mouth, cheek, lips, or the vulva in debilitated and ill-nourished children between the ages of 2 and 6 years, either at the close of some exhausting illness or during convalescence from one of the specific fevers, especially measles, scarlet, and typhoid. (Fig. 11.) *Owing to*

improvement in hygiene, and the care which is now generally given to children's teeth, the disease is gradually but surely becoming a rare one. Its pathology has not been accurately determined, inasmuch as no specific micro-organism has been isolated, but, though the presence of myriads of bacteria within the oral cavity renders the problem somewhat difficult, pathologists are now inclined to regard the *Streptococcus pyogenes* as the causative agent. In all probability the organism, whatever its nature may be, does not become pathogenetic until a certain degree of tissue necrosis has been reached, for though numbers of children suffer from ulcerative stomatitis, only a very few develop



Fig. 11.—Case of cancrum oris. Drawn from a photograph taken after the removal of the sloughs, etc., but before healing had commenced. The patient recovered.

cancrum oris. There can be no doubt that the gangrene is due to the action of bacterial toxins, for it spreads with such a rapidity that limiting inflammatory zone has hardly any time to develop.

Symptoms.—The onset of the disease is insidious, and is unassociated with severe symptoms, either local or constitutional. The child eats well, has little pain, and there is only slight pyrexia. As the disease progresses, pain increases, the appetite is lost, the breath becomes intensely fetid, purulent saliva pours from the mouth, the

temperature rises, the pulse becomes very rapid, coma sets in, and death takes place in a few days from septic intoxication or broncho-pneumonia. The condition generally begins as a greyish patch on the inner side of the cheek, the floor of the mouth, or the gums. An ulcer covered with stinking sloughs, and surrounded by a brawny zone, soon develops, the cheek becomes swollen and shiny, and a small white patch appears on the skin. This patch soon becomes black, perforation takes place, and the gangrenous process quickly spreads. In this way the greater part of the cheek may be destroyed, and large portions of the mandible and maxilla may die. Noma vulvæ extends in a like manner, and may cause a deep ulcer, which spreads towards the rectum, the bladder, or the pubes. Occasionally a similar form of gangrene attacks the scrotum of little boys and the umbilicus of *infants*.

Treatment.—This must be both prompt and heroic. The whole of the gangrenous area, including soft parts and bone, must be clipped away with scissors and forceps until a surface which bleeds at every part is exposed. The walls of the cavity left by removing the slough are then thoroughly seared with the actual cautery, or freely swabbed with pure phenol or fuming nitric acid. If the latter is used, means must be taken to prevent inhalation of the fumes by temporarily plugging the faucial aperture with a sponge; after three or four minutes the action of the acid must be arrested by the application of carbonate of soda When the child is comatose, an anæsthetic is unnecessary. The mouth should be well opened with a gag and the head kept low, to prevent the inhalation of blood and sloughs. A copious dressing of cyanide gauze is applied, and frequent irrigation with a 4-per-cent. solution of permanganate of potash carried out until healing is well advanced. Later the stoma must be closed by some form of plastic operation, a procedure which may tax the ingenuity of the surgeon to the utmost.

4. **Phagedæna.**—This is a form of gangrene which ravaged camps, prisons, and hospitals in pre-antiseptic times. It is a contagious disease, probably caused by an anaerobic bacillus or a streptococcus, which gains entrance through a wound or an abrasion. It spreads with great rapidity, and invariably causes death either by septic intoxication or by hæmorrhage from ulceration into a large vessel. After an incubation period varying from eight hours to three days, the disease develops in either an ulcerative or a gangrenous form. The first is characterized by the presence of a pulpy, greyish, fetid membrane, beneath which ulceration spreads with great rapidity. The second form progresses even more rapidly, and may cause death in less than forty-eight hours. The edges of the wound are everted, glazed, and dusky red, while the surface is

covered with a thick, dark, putrid mass of sloughs and blood-clot. *The intense inflammatory reaction radiates along the connective-tissue planes and leads to extensive sloughing of skin, muscles, and not uncommonly of vessels.* Constitutional symptoms are very severe, fever, diarrhœa, and delirium preceding coma and death.

Treatment.—The contagious nature of the disease necessitates isolation of the patient amidst hygienic surroundings at the first sign of its appearance. Dressings must be burned as soon as they are removed, and every possible precaution taken to prevent spread of infection by instruments or attendants. Nourishing food and stimulants should be freely administered *Local treatment* consists in removing the sloughs and searing the affected area with a cautery. In former days Ricord's paste, a mixture of sulphuric acid and charcoal, was a favourite application In the event of an extremity *being attacked, whenever feasible early amputation well above the* disease is urgently called for.

VI. GANGRENE DUE TO DIABETES

Diabetic gangrene is in reality a form of senile gangrene exhibiting certain differences that depend on the presence of glucose in the blood. Thus, it spreads with greater rapidity, is associated with more surrounding inflammation, has less tendency to self-limitation, and, though often dry at first, generally becomes moist in consequence of the inflammatory changes. Like its prototype, it frequently occurs in old people, begins in the toes, remains limited to the foot or spreads up the leg, and is often started by a slight injury. The most important factor in its production is the narrowing of the *vessels from degenerative and proliferative processes,* occurring either as a purely senile change coincident with diabetes, or as a result of the circulation of sugar. Convincing proof of the etiological importance of arterial changes is afforded by the freedom from gangrene experienced by young diabetics, and also by the fact that, in an analysis of 26 cases of diabetic gangrene admitted to St. Thomas's Hospital, Wallace noted that 24 had arterio-sclerosis, 22 were males, and the average age was 60. Predisposing causes may be the lowered vitality of the tissues in diabetics (thereby rendering them less able to resist injury), the favourable medium that such tissues furnish for the development of pyogenetic organisms, and the occasional defective innervation of the part.

Symptoms.—Diabetic gangrene may be divided into aseptic and septic varieties. The former is dry, non-inflammatory, of rare occurrence, and, apart from the coexisting symptoms of diabetes, does not differ from senile gangrene. The latter and usual type is inflammatory, moist, and septic; it is characterized by its rapid spread, by the

excessive inflammation associated with it, and often by extensive sloughing of the skin. Frequently, following an attack of acute pain, the toes or foot become swollen and œdematous, and dusky red from passive hyperæmia. After remaining in this condition for a couple of days, the swelling subsides, the tissues begin to shrivel, and a black gangrenous patch appears on the toe or foot. This may remain localized, in which case a zone of active hyperæmia develops in the living part and a line of separation associated with a considerable degree of inflammation gradually forms. Such a termination is uncommon. More often the initial swelling and œdema persist, the surface becomes mottled, bullæ form, and septic moist gangrene develops. This quickly spreads up the leg, and is accompanied by a severe degree of inflammation in the adjacent living tissues. While this is taking place the constitutional symptoms of septic intoxication are marked, and frequently accentuated by the glycæmia. If radical measures are delayed, death takes place from septic complications, diabetic coma, or exhaustion.

Treatment.—*Prophylactic* treatment must be directed towards the suppression or reduction of the sugar excreted. This can only be successfully accomplished by a proper diet from which all starchy foods, sugar-producing substances, and sugar itself are excluded, and by the administration of codeine in gradually increasing doses. From the surgical point of view the feet and legs must be kept warm, and the patient should be specially cautioned against the danger of local injuries as an exciting cause of gangrene. Should he sustain a cut or an abrasion, every possible precaution should be taken to secure primary union by rest of the part and by the employment of dry sterilized dressings.

Local treatment.—As soon as the gangrenous process has shown itself the surgeon should endeavour to maintain, or convert it into, the dry variety by promoting asepsis, and should encourage self-limitation by assisting the circulation in the adjacent living tissues. To this end the devitalized area should be swathed in dry sterilized dressings, the limb elevated, and gentle friction applied to the healthy skin. In every case an endeavour should be made to convert a septic process as far as possible into an aseptic one, in order to aid the formation of a line of demarcation. The amount of urine passed in the twenty-four hours must be measured, and the quantity of sugar estimated. If no line of demarcation forms, and if the quantity of sugar does not diminish in spite of a rigid diet and absolute rest, amputation is the proper course to adopt. In cases of non-inflammatory gangrene it is permissible to await a line of demarcation before deciding on amputation, for by so doing the limb may be safely removed at a lower level; but if the patient's constitutional condition

is feeble, or if the percentage of sugar remains high, early amputation should be performed, even though a line of separation is apparently about to develop. In the inflammatory form of diabetic gangrene expectant treatment is dangerous, and therefore not permissible. Whenever possible the operation should be performed under local or spinal analgesia. The tissues should be handled as little as possible, particular care being taken not to damage the flaps with the saw. The technique should be aseptic rather than antiseptic, for chemical substances that are strong enough to be germicidal are also strong enough to kill the tissues. Hæmorrhage is best controlled by digital compression of the main artery in order to avoid damage to the tissues by the tourniquet. If during section of the limb the small vessels do not bleed freely, the amputation should be performed immediately at a higher level. With regard to the site of amputation, most surgeons are now agreed that it is better to amputate above the knee, and thereby secure primary union, than by section below the knee to obtain a longer stump in which suppuration or gangrene of the flaps is liable to occur.

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WOUNDS AND WOUND TREATMENT

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The term "wound" may be defined as a solution of continuity of the tissues, and would, therefore, include all subcutaneous injuries, such as bruises, fractures, etc., as well as the lesions accompanied by rupture of the surface. *It must be remembered that many* injuries present mixed features; thus, an open incision may be surrounded by considerable subcutaneous bruising, a perforation is frequently also lacerated, and so on. It is convenient, however, to describe wounds under the following headings:—

I. **Subcutaneous**—*not accompanied by obvious or immediately* adjacent breach of surface: 1. Bruises and hæmatomas. 2. Sprains (*see* article on Joints, Vol. III.). 3. Fractures (*see* article on Bones, Vol. III.). 4. Ruptures of muscles, nerves, vessels, and solid viscera (*see* under the affected organ). 5. Ruptures of hollow viscera into body cavities (*see* under the affected organ).

II. **Open wounds**—communicating with the surface: 1. Incised wounds. 2. Punctured, gunshot, perforating wounds. 3. Fissures. 4. Abrasions. 5. Lacerated wounds. 6. Contused wounds. 7. Friction wounds. 8. Burns (*see* p. 309) 9. Bursting wounds; for example, by the pointing of abscesses, bursting of gummas, etc.

I. SUBCUTANEOUS WOUNDS

1. **Bruises and hæmatomas.**—A bruise implies injury to the subcutaneous tissues, or to the subjacent organs, due to impact *against any blunt object, and constantly involves multiple* lesions of the blood-vessels; nerve and other tissue elements are torn and damaged to a greater or less extent, but the chief injuries are to be seen in the smaller blood-vessels, which are ruptured and permit the extravasation of blood and serum into the tissues immediately surrounding them.

The part becomes swollen, tender, sometimes painful, especially on movement, and in process of time shows a play of colours due to

staining with blood-pigments and their subsequent oxidation. Thus within a few hours the colour becomes dusky red, and passes thence through the stages of purple, bluish-black, brown, green, and yellow.

The time required for return to normal colour, in a case that remains aseptic, varies with the size of the bruise, the degree of violence that caused it, the reactive powers of the tissues, and the treatment adopted. It is, therefore, impossible to make dogmatic statements as to the age of a bruise from its appearance.

In severe cases, blebs may be formed on the surface, which may contain clear serum or blood-stained fluid, or extensive necrosis may result, with the separation of sloughs.

The degree of bruising from an injury of given violence varies both with the part and with the individual affected Thus, while in a part in which the vessels are badly supported in a loose connective-tissue stroma, as in the eyelid, a slight blow may cause considerable extravasation, in another with a dense structure, such as the scalp, very severe trauma may show but little sign. Also, individuals of flabby, atonic habit and fair complexion will bruise on the slightest provocation. An important fact is that the extravasation may appear at a distance from the site of injury, guided partly by the arrangement of the fascial planes and partly by gravity. Thus, in injury of the scalp the bruising may appear in the eyelids, although these have not themselves been subjected to direct violence; or extravasation due to trauma in the upper part of the leg may show itself as a discoloration round the ankle. In a healthy patient the part usually soon returns to the normal, but in the unhealthy suppuration may ensue.

Bruises of internal organs are dealt with in the articles on the organs affected.

When the trauma causes the rupture of larger vessels, especially veins, or in cases in which the leakage is prolonged for any reason, instead of the diffused hæmorrhagic infiltration seen in an ordinary bruise there may result a definite tumour, separating the tissues and consisting of a circumscribed collection of blood, which later may coagulate, partially or completely. Such a blood-tumour is known as a **hæmatoma**. In those cases in which partial clotting occurs the coagulum is especially deposited in the peripheral parts of the cyst, the central parts being occupied by a more or less fluid content. This condition is of particular interest in the skull, owing to its simulation of a depressed fracture

A hæmatoma may terminate in one of four ways: (1) It may become gradually and entirely absorbed; (2) it may suppurate, if infected by organisms which gain entrance either through the abraded surface or by the lymph- or blood-stream; (3) by disappearance of

its fluid centre it may leave a firm and persistent mass; or (4) it may lead to the production of a permanent cyst with hæmatoidin-pigmented walls and a clear fluid content. The absorption of a hæmatoma may be associated with a considerable degree of pyrexia, sufficient perhaps to cause suspicion of suppuration.

TREATMENT OF SUBCUTANEOUS WOUNDS

Bruises.—Treatment should be directed to stopping the subcutaneous vascular leakage, to relief of pain, and to acceleration of the absorption of the extravasated and damaged material. *Rest is important both for the relief of pain and for the prevention of* swelling. *Elastic pressure* is of great value during the very early stages for the inhibition of excessive extravasation, but should be used with caution when definite swelling has been established. *Cold applications*, in the form of douches, ice, or evaporating lotions; heat, and the use of *local anodynes* such as lead lotion, belladonna, or glycerine and atropine, may serve to allay pain. Although lead salts are powerfully astringent and to a certain extent anodyne, probably the chief value of lead lotion when applied to unbroken skin is attributable to the cold induced by its evaporation. Heat should only be applied when all danger of increasing the extravasation has passed. In the later stages *massage* is of great value for the promotion of absorption, and even from the first a gentle form of effleurage (stroking) and pétrissage (kneading) is very comforting to the patient.

Hæmatomas must be treated on the lines indicated above, which will usually lead to entire absorption. Occasionally the removal of an unduly large hæmatoma may be facilitated by incision and evacuation, under rigidly aseptic precautions. Old cysts or fibrous tumours resulting from hæmatomas will require excision, while suppurating blood-tumours must be treated as abscesses, incised, emptied and drained.

II. OPEN WOUNDS

1. An **incised wound** is a clean-cut linear wound, usually not associated with much bruising of the edges. It bleeds freely owing to the fact that the coats of the vessels do not retract so much and are not so broken up and roughened as when torn or crushed. It is caused by any sharp instrument. Sometimes, as in the case of truncheon wounds, it may be the result of splitting of the soft tissues between a blunt instrument and a flat, bony surface such as the skull, the patella, or the shin.

Incised wounds may be divided into those in which pathogenetic organisms may be expected to be present, and those in which there is

a fair presumption of their absence, as in "clean" wounds deliberately made by a surgeon.

2. **Punctured wounds** are caused by bodies penetrating either from without or, as in some compound fractures, from within. Their chief characteristic is their depth as compared with their superficial extent, so that a quite small external wound may lead to an extensive internal injury. Owing to the length of the track and the tendency for the superficial parts to close more quickly than the deeper, these wounds are especially liable to tension and suppuration. Moreover, sometimes either the whole or a part of the penetrating instrument remains embedded, e.g. needles, pieces of cloth, etc.

Gunshot wounds are punctured wounds of a special character, for a detailed consideration of which reference must be made to special textbooks.

Perforating wounds are sometimes considered as a subdivision of punctured wounds, and taken to mean those in which the lesion extends to one of the body cavities.

3 A **fissure** is a splitting wound, often due to over-extension or over-distension.

4. An **abrasion** is a very superficial laceration only affecting the skin or mucous membrane, cornea, or conjunctiva.

5. **Lacerated wounds** are caused by dragging or tearing, e g. by machinery or by blows against rough surfaces. They are frequently associated with contusion. The wound has irregular and ragged edges, and is always deeply soiled with ground-in foreign particles. Unlike punctured wounds, the superficial area, except in cases of complete avulsion of a limb, is large in proportion to the depth. The wound has many shreds which, being deprived of their blood supply, tend to necrose in a greater or less degree.

Hæmorrhage is comparatively slight, owing to speedy retraction of the roughly torn vessels. The prevention of suppuration is difficult, on account of the damaged and dirt-engrained condition of the tissues. Owing to the necessity for the removal of the injured tissues, healing by granulation is the rule.

6. A **contused wound** is brought about by injury with a blunt instrument, and only differs from a laceration in that the bruising element predominates over the tearing.

7. **Friction wounds** combine the characteristics of laceration and burning; the wound caused by a rope rushing through the hands may be taken as an example. They are usually painful, and slow to heal.

TREATMENT OF OPEN WOUNDS

The wounds inflicted by the surgeon will be discussed under the heading of Surgical Technique (p. 301).

Treatment of accidental wounds necessitates attention to the following points:—

i. Stoppage of hæmorrhage.
ii. Cleansing.
iii. Investigation.
iv. Coaptation, if possible.
v. Drainage, if necessary.
vi. Rest.
vii. Maintenance of general health.

i. **Stoppage of hæmorrhage.**—It is very important that bleeding should be stopped, for, apart from the possibly disastrous results of continued hæmorrhage, such unchecked bleeding materially interferes with healing by preventing coaptation of the edges of the wound, by providing a nidus for the development of micro-organisms, and by preventing adequate examination of the relationships of the wound, especially in its depths. The drier the wound, the more likely is primary healing without infection.

Temporary arrest of hæmorrhage is called for in cases of urgent bleeding, and may be effected by several methods:—

(*a*) Pressure at the site of hæmorrhage is the first and immediate course to be adopted. Even extremely alarming bleeding may be efficiently controlled by the prompt local application of the thumb, a pad, or a firm bandage.

(*b*) Pressure between the bleeding-point and the heart. For example, in large arterial wounds proximal pressure is brought to bear by digital compression or some form of tourniquet, improvised if necessary. In venous hæmorrhage, on the other hand, it is important that no proximal compression be employed, for if only sufficient force be used to obliterate the veins but not the arteries, the bleeding will be encouraged rather than stopped. Local pressure is quite effectual in such cases, as a temporary measure.

(*c*) Packing with gauze or wool is often useful, especially when the blood wells up from a deep wound, or from a sinus in the skull. Its value is largely dependent on the local pressure exerted, but also, to some extent, on its action in promoting the formation of the external clot. Even apparently serious hæmorrhage can be readily controlled temporarily by this means. It is not advisable, however, to rely upon packing as a means of permanent hæmostasis, inasmuch as primary healing is prevented by the presence of the gauze or wool, and further hæmorrhage may follow its removal.

(*d*) Forceps should be applied to the bleeding-points only; but sometimes in an emergency, when the actual vascular opening is not immediately obvious, it is justifiable temporarily to include some of the surrounding tissues in their bite. Many forceps have been

devised, but those of Lawson Tait and Spencer Wells are the best adapted to the purpose.

Permanent hæmostasis sometimes follows naturally the temporary measure, but usually other manœuvres are necessary, such as—

(*a*) Ligation of the open vessel, care being taken to avoid inclusion of excess of surrounding tissues.

(*b*) Ligation of the vessel in continuity.

(*c*) Suture of the wound in such a manner as to include the bleeding-point is often of value, e g. in bleeding from the frænal artery of the prepuce, also in association with pressure by firm dressings, as in bleeding from the scalp, where the vessels are difficult to pick up.

(*d*) Torsion, by lacerating the inner coat of the vessel, promotes hæmostasis, and is of value for comparatively small vessels in that it does not involve the presence of a ligature, i.e. a foreign body, in the wound.

(*e*) Acupressure.

(*f*) Hæmostatics, such as adrenalin or hydrogen peroxide, may be employed, especially in cases of general oozing. They are, however, unsatisfactory. In the case of adrenalin the vaso-constriction is followed by vaso-dilatation, so that the hæmorrhage is merely delayed.

(*g*) Heat and cold. Heat is a more efficient hæmostatic than cold, and may be applied in the form of hot water at a temperature of 120° F., or of the actual or galvano-cautery at dull-red heat. Warm water below 118° F., on the other hand, will encourage bleeding.

ii. **Cleansing.**—In the first place the wound itself should be covered with a clean dressing, and attention directed to the thorough cleansing of its surroundings. This is effected by shaving, by the free use of soap and water, followed by grease solvents such as ether or turpentine, and by antiseptics such as alcohol, mercurials, lysol, or carbolic. The wound is then uncovered, washed, freed from foreign particles and lacerated shreds, and swabbed out with antiseptics such as hydrogen peroxide, carbolic, mercurials, lysoform, etc. Or the surrounding skin may be cleansed with acetone and then painted with iodine, without the preliminary use of water.

iii. **Investigation** is necessary to ascertain the extent of the wound, to facilitate discovery and removal of foreign bodies and fragments of clothing, and to ensure recognition of damage to important structures such as nerves, vessels, tendons, bone, and adjacent joints and body cavities. Thorough examination of the nerves and their areas of distribution before the patient is anæsthetized will enable the surgeon not only to give a more accurate prognosis, but also to adopt measures for their repair; whilst in the skull special care is necessary to ensure detection of fractures, if present. The question

of the amount of exploration desirable in wounds over joints is one of considerable difficulty. A definite rule, however, must be laid down that in no cases are such wounds, especially if punctured, to be probed, for this procedure is apt to entail soiling of a joint which otherwise might have escaped infection. If the wound has been inflicted with a fairly clean instrument, and if joint-involvement be either problematical or of slight character, as demonstrated by the escape of a drop or two of synovial fluid, it is advisable to temporize, i.e. to cleanse the more superficial parts thoroughly, to attempt no immediate definite exploration, but to await evidence of infective joint-involvement, such as rise of temperature, local heat and redness, effusion into the joint, pain and limitation of movement, or other indications for interference. It must be remembered, however, that any trauma in the region of a joint may give rise to a non-infective synovial effusion into the subjacent articular cavity. If, on the other hand, the wound into the joint be certain and fairly extensive, and the instrument be undoubtedly dirty, immediate open exploration is advisable.

The experience gained in the War has shown that accidental wounds are best treated by immediate excision of the tissues that have been exposed to infection; this method not only removes the greater number of the organisms that have entered the wound, before they have multiplied and spread, but also the damaged tissue, which is so favourable a nidus for their growth. In such circumstances the wound may sometimes be sutured and healing by first intention may be obtained; but inasmuch as it is impossible to be certain that infection has been abolished, it is better to pack the wound in all its interstices with flavine-soaked gauze, and then on the second or third day (i.e. before granulations are established) to remove the gauze and suture completely if infection be absent. Suture performed at this time is commonly known as *delayed primary suture*; if done at a later date, after the establishment of granulations, the term *secondary suture is applied.*

The same general rules may be laid down for the treatment of wounds suspected of involving the peritoneum.

Careful examination is also necessary to discover the presence and position of foreign bodies, such as needles (p. 283), pieces of broken tool, and glass.

iv. **Coaptation** of the wound surfaces and edges is to be carried out by one of the methods described hereafter. Accurate closure must only be adopted when cleanliness and dryness have been ensured. It is usual, therefore, not to stitch up punctured or extensively lacerated wounds closely; room must always be left for efficient drainage.

v. **Drainage.**—A drain should be used—

(*a*) When doubt exists as to efficient removal of infective material; for example, in punctured wounds.

(*b*) When effective hæmostasis is not obtainable.

(*c*) When, owing to severe laceration or contusion, some necrosis is expected.

(*d*) When it is impossible to avoid the existence of an actual or potential cavity in the deeper layers of the wound in which serum or blood may accumulate.

We must here draw attention to some fallacies in draining that have in the past defeated the very object of the process. Too often, especially in the abdomen, has the tube been kept in unnecessarily long, for after a short time, from twenty-four to forty-eight hours, the general abdominal cavity becomes entirely shut off by adhesions, so that after that period the surgeon is not draining the general cavity but merely the track of the drain. Moreover, the tube prevents the closure of the track, which, therefore, forms a path for secondary infection from the skin. Suppuration from its walls is induced, and the simple drainage track is converted into a sinus exuding pus and demanding treatment which protracts the convalescence.

For a similar reason it is advisable to avoid drainage of abscess cavities due to pure tuberculous or, in many cases, pure pneumococcic infection Secondary infection, usually by the staphylococcus, enters along the track and may lead to long-continued suppuration with its sequelæ, amyloid degeneration and exhaustion.

Modern surgery, therefore, aims rather at emptying such cavities, treating their walls by gentle curettage, by applications of iodine, iodoform, or other antiseptic, and by careful closure of the incision. This process may need to be repeated, but it is greatly preferable to the long-continued drainage which was formerly employed.

Drainage may be accomplished by the agency of strands of salmon-gut, horsehair, or similar material in the case of small wounds in which but little effusion is expected, or in larger collections by the use of tubes of indiarubber, glass, celluloid, or metal, in which lateral holes or slits have been made

Precautions must be taken to prevent pressure against vessels by any rigid, or especially any strongly elastic, drainage material; in the presence of infection such pressure may cause ulceration of the vessel wall and secondary hæmorrhage.

Gauze wicks are sometimes employed, either alone or as a central strip down the lumen of the drainage-tube, with a view to assisting the removal of the fluid by capillary suction. Care, however, must be taken to ensure by loose packing that they act as wicks and not as plugs. A useful variety is the cigarette drain, which consists of alter-

nating layers of gauze and dental rubber or protective. It is made by laying a square of gauze upon a square of protective and then loosely rolling them together in the manner of making a cigarette.

In those wounds that are certainly or presumably infected, the Carrel-Dakin method of wound treatment is to be strongly recommended. It is primarily a method of applying a powerful antiseptic to the depths of a wound, but it also favours drainage After complete investigation of the wound and provision of adequate drainage small rubber tubes (Fig 12), which are closed at the distal end and punctured laterally with punch holes, are distributed over the wound, the number of tubes depending on the size of the wound; they are so arranged that when the fluid is injected it escapes through the

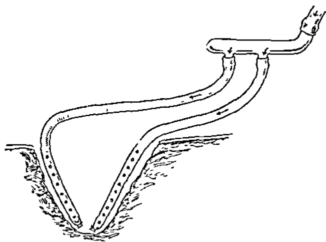


Fig. 12 —Carrel's tubes.

lateral holes in the tubes and reaches every corner of the raw surface; the tubes are maintained in position by a light packing of sterile gauze, and the Dakin fluid is injected at two- to four-hourly intervals in an amount sufficient to cover the raw surface thoroughly, without overflowing. The surrounding skin should be smeared with sterile vaselin to prevent irritation by the solution; it is important to see that the lateral holes in the tubes are all within the wound and not lying against the skin. The whole wound is then covered with a mass of absorbent wool, and outside that with non-absorbent wool, the latter to prevent soaking of the bed. The result is an intermittent instillation (not irrigation) of Dakin's solution into the wound. This fluid gives off free chlorine and is bactericidal; clinically, the striking feature is the rapidity with which necrosed portions of tissue are removed, and consequently the speed with which the bacterial content of the wound is reduced. Carrel controlled the method by taking smears from the wound and counting the average number of micro-

ganisms seen in a microscopic field; if the number seen was less an one to the field, he regarded the wound as "clinically sterile" d fit for secondary suture. In doing secondary suture, the skin ges should be excised, the deep parts of the wound obliterated by arded mattress sutures, and the skin edges accurately apposed. The ccess following secondary suture is greater if the wound can be renred "clinically sterile" within ten days of its infliction; after that ne the results are so variable that it can hardly be recommended.

vi. **Rest.**—Rest, both of the patient and of the affected part, y posture, splints, accurate suturing and bandaging, etc, is obviously ecessary.

vii. **Maintenance of the general health** must also ceive attention.

NEEDLES, ETC., IN THE TISSUES

The localization and removal of sharp-pointed bodies, such as eedles, from the tissues may be a matter of ease. Frequently, owever, even with the aid of the X-rays, it involves tedious and xtensive dissection, often amidst important structures; for example, n the palm of the hand Prolonged attempts, therefore, should not e made without careful radiographic localization. In view of the act that a needle may travel through a comparatively great distance n a short time if movement of the affected parts has been permitted, he operation should be performed as soon after the radiogram has een taken as possible It must be remembered that with a single hotograph it is difficult to determine the exact plane and direction n which the needle lies. Reliance upon this method, therefore, may ead one, in the first place, to cut down upon the palm when really he needle lies posteriorly to the metacarpals, and in the second place, o form an inaccurate judgment of its size owing to foreshortening y obliquity. Hence it is desirable in all cases that two views be aken, either in planes at right angles to one another or in stereocopic register Perhaps the best method is to conduct the operation n the X-ray room so that advantage may be taken of the fluorescent creen. An accurate impression of the position and size of the foreign ody may be obtained by studying the part from all points of view with the screen, note being taken of the relative extent of movement of the bones and the needle on rotation of the part. Sometimes another needle can be introduced and made to touch the embedded one; if so, an excellent clue is obtained to its whereabouts, and the operation is materially facilitated.

AMPUTATIONS FOR INJURIES

Modern surgical methods, by eliminating many of the risks of sepsis and by reducing shock, have greatly modified the certain

indications for amputation for injury. Primary amputation, that is, one performed immediately after an injury or as soon as the shock has passed off, is *certainly* called for in cases of avulsion of a limb, of complete "pulping," or of absolute destruction of both the arterial and venous supply to the part. Extensive laceration of the skin, or damage to the main vessels, nerves, and bones, is not now to be regarded as a sufficient reason for primary amputation in a part otherwise healthy, for skin-grafting, vessel- and nerve-suture, bone-grafting, and other conservative measures will frequently permit the retention of a useful limb.

The surgeon must therefore take into consideration the general health, age, and constitution of the patient, and the probable subsequent value of the limb. An old or debilitated subject is more likely to bear the comparatively short convalescence from an amputation which heals by first intention, than the protracted and wearisome recovery which follows the adoption of conservative methods, especially if they require a recumbent position with its attendant dangers of hypostatic congestion of the lungs, pneumonia, etc. Again, a patient in poor circumstances is frequently better off with a stump capable of adjustment to an artificial limb than with a longer and more or less mutilated member requiring long-continued care.

Every effort must be made to save parts of an upper limb, especially the thumb and fingers, inasmuch as no artificial substitute performs their delicate duties so satisfactorily as even a damaged hand and arm, while the lower limb, which chiefly serves for support, is readily replaced by a comparatively simple apparatus

Secondary amputation is required in cases in which sepsis has supervened and is progressive, in which gangrene has occurred, or in which the limb resulting from conservative measures proves to be useless or even detrimental to the patient.

Amputations for infective conditions, or in which the wound is likely to become infected, should be left widely open with flaps turned back to permit the freest possible drainage; then, depending on the rapidity with which clinical asepsis can be secured, the stump may be covered by "delayed primary" or by "secondary" suture. While the flaps are thus left open, retraction must be prevented *by strapping* and extension.

SURGICAL TECHNIQUE

Introductory and historical.—It is unnecessary to compare modern surgical results with those achieved in pre-Listerian days. The enormous advances due to the recognition and the application to surgery of the work of Pasteur and other investigators of the germ theory of disease, and to the adoption of Lister's methods,

are a matter of common knowledge. Lister's methods implied the free use of powerful antiseptics designed to kill or inhibit the growth of infective organisms.

To a certain extent these chemicals, necessarily irritant, are still in everyday use, but experience has now taught us (1) that some of these lotions (e.g. perchloride of mercury) are comparatively inefficient in the body owing to their interaction with its proteins, and (2) that owing to their irritant character they devitalize and lower the resistance of the normal tissues to infection.

There is now a general tendency, therefore, to adopt measures to exclude micro-organisms by the thorough thermal sterilization of all material brought into contact, directly or indirectly, with the tissues, and to limit the use of antiseptics to disinfection, so far as is possible, of the skin of the surgeon and of the patient Even here, in the practice of many surgeons, these chemicals are relegated to a secondary position as compared with thorough cleansing with soap and water.

Surgeons of the "antiseptic" school trust mainly to chemical methods, while those of the "aseptic" prefer to rely chiefly upon mechanical and thermal means of sterilization.

Basis.—The general principle underlying modern surgical technique is that *all infection of wounds is derived from without*, it being understood that "without" must be taken to include almost all the mucous cavities as well as the external surface of the body. Technical details are planned on the assumption that normal unexposed tissues are sterile, and that therefore in practice auto-infection occurs so rarely as to be negligible.

Among the extraneous potential sources of infection are included all materials that may be brought into contact in any way with the wound or its surroundings.

Sources of infection.—It is advisable at this point to consider briefly the common paths of infection in a case not previously infected.

1. The skin of the patient, and of the surgeon and his assistants, is probably at once the most prolific cause of defilement, and the one [illegible]

must be confessed that ideal surgical cleanliness of the skin has not yet been attained.

2. The clothing of the patient, and also that of the surgeon and his assistants, should be of material that admits of sterilization by heat.

3. The mucous membranes of the patient are, as a rule, to be considered infective, but it must be remembered that in a healthy person the following parts are sterile:—

i. The mucous membrane of the nose and its accessory sinuses, except in the inferior meatus.

ii. The middle ear and its adjacent cavities.

iii. The stomach and duodenum, which in health contain practically no infective organisms. Those ingested are rapidly destroyed by the free HCl.

iv. The urinary tract down to the bladder, and in men probably the bladder itself.

v. The body of the uterus and the Fallopian tubes, which are normally free from organisms, though the cervix is not.

But since operations are, as a rule, performed on all these mucous membranes when in an unhealthy condition, they are for practical purposes to be considered as infective.

4. Instruments.

5. Lotions.

6. Dressings, sutures, ligatures, etc.

7. *The air.* Although in the early days of the Listerian procedure this was regarded as a frequent and dangerous source of infection, it is now proved that in the absence of draughts, dust, and particles of moisture, such as droplets of saliva expelled by talking, sneezing, or coughing, the atmosphere of the operating theatre does not convey pathogenetic organisms. In a well-regulated theatre, therefore, so few organisms gain entrance in this manner that they are negligible

METHODS OF STERILIZATION

1. **Mechanical and solvent.**—Clipping and scrubbing, combined with the use of soaps, ether, petrol, turpentine, and other grease solvents.

2. **Chemical.**—Antiseptic solutions, vapours, and pastes.

3. **Thermal.**

i. Dry heat:
- (*a*) Actual cautery.
- (*b*) Flames.
- (*c*) Hot air.

ii. Moist heat:
- (*a*) Boiling.
- (*b*) Steam—
  - α. At rest, at 100° C., not under pressure and not so saturated as β.
  - β. In motion, at 100° C., and not under pressure = ordinary live steam.
  - γ. Superheated steam (not so saturated as δ).
  - δ. Steam under high pressure.

1. The **mechanical and solvent** methods are all-important, and practically must never be omitted as a preliminary to any other form of disinfection. Sterilization of the skin by the strong alcohol and the iodine methods is the one exception to this statement.

2. The **chemical methods** depend on the use of the various antiseptic lotions and vapours, which will be discussed later.

3. **Thermal.**—i. Dry heat is considerably less germicidal than moist heat of the same temperature, and therefore has been largely superseded. Occasionally the flame is used for the rapid disinfection of small instruments, such as vaccination tools, platinum loops, etc., or for bowls and similar utensils.

ii. Moist heat.—(*a*) *Boiling* for twenty minutes in water or, better, in a 1-per-cent. solution of sodium bicarbonate or sodium biborate, is the method usually applied to instruments. Soda or borax not only prevents the tarnishing of the steel caused by boiling in plain water, but also raises the boiling-point of the fluid to 104° C. It is essential that the instruments should be completely covered with the solution, and that the lid be kept on the pot or sterilizer in order to prevent excessive loss of heat by evaporation from the surface.

Even sharp instruments may be boiled if their edges be carefully protected with lint or cotton-wool. Undoubtedly, however, frequent boilings do impair their temper, and therefore many surgeons content themselves with immersion of knives in spirit or pure carbolic for half an hour or more.

(*b*) *Steam.*—(*a*) Steam at rest is less efficient than live steam, and is not now used.

(*β*) Live steam (steam in motion) affords a valuable disinfecting agent, especially for gowns, towels, dressings, and other fabrics. Various sterilizers have been devised; among the best-known are Schimmelbusch's, Lautenschlager's, and Stack's.

The kettle is packed with the materials to be sterilized, and placed, with its apertures open, in the sterilizer, which is then closed. The steam is admitted and allowed to circulate for an hour. After the contents have dried by evaporation the apertures are closed by means of the sliding plates, and the kettleful of dressings is ready for use.

(*γ*) The use of superheated steam involves the provision of elaborate machinery, and does not give results so good as those of steam under pressure.

(*δ*) Steam under pressure affords the most satisfactory method, [illegible] jected to steam at a pressure varying from 10 to 20 lb. for 15 to

operating room, in this country most surgeons content themselves with less drastic methods, apparently without detriment to the aseptic result. The surgeon, having put on over-boots and mackintosh apron, if it be his custom to use them, proceeds to cleanse and disinfect his hands and arms thoroughly by the methods detailed above. Then from a sterilizer drum, held open for him by one of his assistants, he takes a sterilized overall and puts it on, being careful to avoid any contact with its outer surface. A sterilized cap and mask having been fastened on, he proceeds to the process of gloving. He must first assure himself that the gloves are free from needle punctures; then, avoiding all handling of their outer surface with the naked hand, he seizes the everted wrist of the glove and draws it on as far as possible by gentle traction, completing the accurate fitting by stroking the fingers upwards with sterilized gauze. If gloves sterilized wet be used they may be floated on while full of lotion, or pulled on after wetting the hands with spirit; if dry gloves—which we prefer—be employed, they should be powdered inside with sterilized talc and drawn over the thoroughly dried and powdered hands; the powder should not be used in such quantity as to form a definite deposit inside the glove

Any moisture must now be squeezed out, and the sleeves of the garment introduced beneath the wrists of the gloves; the surgeon is then ready to begin work.

PREPARATION OF THE PATIENT

The patient should, if possible, be under observation for forty-eight hours before operation, with a view to thorough general examination and record, and also to accustom him to his surroundings and to confinement in bed. During this period the bowels should be cleared out and the oral hygiene attended to. The teeth should be scaled and cleaned, and the mouth systematically washed out, especially in all operations involving the mouth, jaws, neck, and digestive tract, and in cases requiring prolonged anæsthesia. If this precaution be rigidly observed, the number of cases developing post-operative pneumonia, secondary parotitis, etc., will be greatly reduced. In gastric cases and in cases of intestinal obstruction, especially if stercoraceous vomiting be present, lavage of the stomach should be practised. Its slight addition to the shock is more than counter-balanced by the increased safety of the operative procedure and the lessened risk in the administration of the anæsthetic.

The skin for a wide area round the proposed site of operation may be prepared as follows:—

On two days before the operation the site is shaved for the purpose of removing not only hair, but also superficial epidermis, and then

thoroughly washed with soap and warm water for fifteen minutes The nail-brush should be freely used for all patches of roughened and hardened skin, such as that of the hands, feet, and prepatellar region, but on delicate skins it frequently does more harm than good, by causing abrasion and hyperæmia, and by scrubbing in micro-organisms. The part should then be swabbed over with turpentine and with ether, followed by some efficient antiseptic lotion, and finally covered with weak antiseptic compresses. Warning is necessary against the use of weak carbolic compresses on fingers or toes, for fear of gangrene.

On the evening before operation this dressing is removed and the cleansing processes are repeated, followed this time by dry dressing, or again by a weak antiseptic compress, which is not disturbed until the patient is on the table ready for operation It is then removed, and the part washed over with spirit or other lotion. If the previous cleansing be trustworthy, it seems to us unnecessary to "wash-up" again on the table, as is the practice of many surgeons. In emergency cases, reliance must be placed on thorough washing at the time of operation; and some surgeons are content to depend on such immediate cleansing even in cases where time would permit the longer process.

The method of skin disinfection by iodine is simple, rapid, trustworthy, and especially suitable for emergency operations. A practical point is the necessity for avoidance of the immediate preliminary use of soap and water, which, by causing swelling of the prickle-cell layer, prevents thorough permeation by the iodine

The part should either be shaved twelve hours previously with soap and water, or dry-shaved just before the operation, and then painted with the chosen preparation of iodine. By many the official tincture is used, but this tends to produce an erythema unless it is freshly made. Others use a 1-per-cent solution in benzine (Bogdan), or in benzine and paraffin (Esau) Esau's formula is—

Tinct iodi	10
Benzine	750
Liquid paraffin	250

These formulæ have the advantage of containing an efficient fat-solvent in addition to the antiseptic

Iodine may also be used in chloroform solution (1 : 15), and this possesses the merit of forming a more stable preparation than the tincture.

Acetone also affords a useful method of skin preparation. Acetone, by itself, is a feeble antiseptic. Combined, however, with iodine or with alcohol (equal parts of acetone and 95 per cent. alcohol) it gives excellent results. But it has one drawback: it is intensely irritating to some people, producing profuse lachrymation and coryza.

In order to overcome this difficulty A. J. Wallace has introduced a combination of dichloride of ethylene and iodine which possesses all the solvent without any of the irritating properties of acetone. The use of this combination entirely does away with the need for prolonged cleansing, compresses, etc., and for this reason adds to the mental and physical comfort of the patient. His method is as follows: *About an hour before the operation the area is rubbed over with a mixture of ethylene dichloride and alcohol on sterile swabs. This is followed by rubbing in pure ethylene dichloride. The iodine-ethylene-dichloride mixture (I.D.E.) is then painted over, and the whole covered with a sterile dressing.* The results are excellent.

A 3-per-cent. solution of picric acid in spirit has proved a quite satisfactory substitute for the iodine solutions, and is especially valuable in cases that are sensitive to iodine, e.g. children.

Disregard of the psychical condition of the patient is only too common The surgeon tends to regard the case as one of diagnostic or therapeutic interest, and fails to realize that he has to deal with *a personality as well as with a disease.* To inspire in the patient placid confidence leads to quiet anæsthesia, less shock, and a more satisfactory convalescence. From this point of view the choice of suitable nurses and the control of the *patient's friends are especially* important, and may call for strong but tactful dealing.

The patient should be led to think that the operation is merely an incident in the treatment, and should be discouraged from focusing his whole attention upon it. We believe that the systematic violent purging and rectal lavage formerly so usually adopted, whether specially indicated or not, frequently do more harm by disturbing the mental equilibrium than good by the removal of the maximum of stercoral matter.

The maintenance of the body warmth is *very important*, especially in children, old and feeble people, and the victims of severe trauma. The operation table should be warmed, and the patient warmly clad and surrounded by hot-water bottles, placed with due care to avoid burning during unconsciousness.

The alteration in diet necessitated by the anæsthetic is discussed at p. 728. As a preliminary to operations on the stomach and duodenum it is recommended that, when circumstances permit, for two days before *operation the patient be fed on foods that have be*[illegible]lized.

PREPARATI[illegible] ROOM

1. In hospital.—It is [illegible] in this wo[illegible] modern theatre construction. [illegible]

2. In private [illegible], the cleared, carpets taken up, [illegible]s,

furniture removed. The floors should be washed and the room dusted with moist cloths. Some surgeons have the room disinfected with moist formalin vapour, but, if this be used, thorough ventilation is afterwards essential.

The following should be provided:—

(*a*) A portable operating-table, capable of permitting the raising and lowering of the head, and of giving the Trendelenburg position. Failing this, a narrow but firm kitchen table, or two tables end to end, or in the form of a T, may be used.

(*b*) Three small tables—one for dressings, sterilizer, drums, etc., a second for instrument-trays, and the third for the anæsthetist.

(*c*) Several sterilized bowls and basins.

(*d*) A large supply of hot and cold sterilized water.

(*e*) A convenient instrument sterilizer.

(*f*) A plentiful supply of the chosen lotions (*see* p. 296).

(*g*) Efficient lighting—preferably a natural north light. Also hand-lamps.

(*h*) A couple of washstands, with boiled nail-brushes.

(*i*) Blankets pinned inside clean sheets for laying under and over the patient.

(*j*) A piece of oilcloth to spread under the table.

ii *In an emergency* the less disturbance of the room with a view to cleansing, the better. It is wiser to leave dust on the floor than to stir it up in a hurried attempt to prepare the room. The floor may be covered with damp sheets, but otherwise very little should be done.

PREPARATION OF INSTRUMENTS AND UTENSILS

Sharp-edged steel instruments may be disinfected by immersion for half an hour in methylated spirit, or for 15 minutes in pure carbolic; or they may be boiled in 1-per-cent. soda solution or borax solution for 4 to 5 minutes. The blunting so liable to occur in the latter two methods may be, as we have said, largely prevented by wrapping the blades in cotton-wool or lint to obviate contact with the containing vessel.

Blunt steel instruments are to be sterilized by boiling for 20 minutes in 1-per-cent. soda or borax solution. The addition of the soda or borax (a teaspoonful to a pint) to the water serves the double purpose of preventing discoloration of the instruments and of raising the boiling-point from 100° C. to anything between 104° C. and 106° C. It is essential that the solution be in a state of active ebullition, that the instruments be completely immersed, and that the lid of the sterilizer be in position. Unless the liquid be kept stirred by the process of ebullition, and the lid be kept on to prevent rapid evaporation accompanied by cooling of the surface, the

temperature is not uniform throughout, and is frequently less than 100° C. at the surface. When the process of sterilization is completed the instruments are laid out on a tray, either on a dry sterilized towel, or in sterilized water, spirit, or 1 : 20 carbolic.

Glass instruments, and still more glass-and-metal instruments, such as syringes, are liable to crack if put direct into boiling water, and therefore should be put first into warm water, which is then raised to boiling-point and maintained at that heat for 20 minutes. Injection syringes are frequently sterilized by immersing the needle in and filling the syringe with *oil at a temperature of 160° C. This temperature* may be roughly taken to be that at which bread immersed in the oil is fried brown.

Silver and *rubber catheters* are sterilized by boiling. *Gum-elastic catheters* may be kept in glycerine and perchloride of mercury, or in long test-tubes fitted with caps containing formalin so that the instruments are kept continuously in a moist formalin vapour. Boiling is very efficient, but quickly rots the fabric.

Gloves may be boiled in plain water without soda, or sterilized dry with the dressings. If the latter method be adopted, it is essential that their freedom from holes be first ascertained, and that, in order to prevent sticking together, they be thoroughly dried and powdered. It is our custom to sterilize the gloves, towels for drying the hands, and a castor of talc powder together in a separate small drum.

Bowls and *basins should be boiled in a large copper.* In cases where this is impracticable, the dishes may be "flamed" by rinsing in methylated spirit, which is then set alight. It is obvious that the common fault of handling bowls with the thumb *inside must be* avoided.

PREPARATION OF DRESSINGS, SWABS, SPONGES, ETC.

These should all be made of sterilizable material. The use of marine sponges should be entirely abandoned, owing to the involved processes and uncertain result of their preparation. In their stead, for the packing-off of cavities, e.g. the abdomen, the surgeon may use either rolls of gauze or squares composed of several layers of gauze stitched together and having a tape fixed to one corner, brought out of the wound and caught in forceps, to prevent loss in the abdomen.

For use as mops, swabs made of cotton-wool tied in gauze, or small squares of gauze in several layers, are convenient and completely sterilizable.

We prefer simple, plain gauze and wool to the medicated varieties, such as those impregnated with iodoform, cyanide, or sal-alembroth If these be used, they, like the plain dressings, must be sterilized by *heat, and thus much of* the iodine is driven off slowly from iodoform.

Iodoform gauze for packing is often used in view of the fact that it gives off nascent iodine in contact with pus or blood, but it may set up unpleasant local irritation and general toxic effects.

In similar manner all towels, overalls, and other fabrics are to be sterilized by heat.

LIGATURES AND SUTURES, AND THEIR PREPARATION

Very varied substances have been used for ligature and suture purposes in an endeavour to obtain a material which shall combine all the following characteristics:—

(*a*) It must be absolutely sterilizable.

(*b*) It must retain its tensile strength.

(*c*) It must not be absorbed before it has fulfilled its purpose.

(*d*) It should, however, be absorbable, so that in septic cases it may not remain in the tissues to prolong suppuration.

(*e*) It should be soft and readily flexible, so that it may lie flat at the eye of a needle and not form an awkward bulge requiring a pull to bring it through the tissues.

(*f*) It should be non-irritant.

The materials that have been adopted fall naturally under two heads: (1) the *absorbable*, such as catgut, kangaroo tendon, reindeer tendon, and ox aorta, and (2) the *non-absorbable*, such as silk, linen thread, Pagenstecher's celluloid thread, silkworm gut, horsehair, silver and other wires. It is obvious that an absorbable material is ideal for buried sutures and ligatures, provided that it permits of efficient sterilization. Inasmuch, however, as none of the absorbable substances used can be boiled without change in their properties, the only perfect and convenient method of disinfection, viz. that by moist heat, is applicable only in the case of the non-absorbable sutures.

Catgut satisfies all the above essentials except that it will not withstand disinfection by heat, and that usually it is less flexible than silk or thread of corresponding size. Innumerable ways of preparing catgut have been devised since Lord Lister first introduced the carbolic-oil method, which has been abandoned owing to experimental proof of its inefficacy.

The iodine method of preparation is so simple and so relatively safe that we may dismiss the formalin, biniodide, and perchloride methods at once. Commercial catgut is immersed in ether for 24 hours, transferred to a 1-per-cent. solution of iodine in 1·5 per-cent. potassium iodide for eight days, and is then ready for use. It may be stored in the iodine solution or dry in sterilized bottles. Before use it should be steeped for a few minutes in sterilized water.

Catgut prepared by the iodine method is strong, absorbable, and, in the practice of a great many surgeons, reliably aseptic. It is not

so strong, however, nor so flexible as silk or thread, both of which possess the *additional advantage that they can be boiled*. Moreover, Richardson has collected 21 cases of postoperative tetanus following the use of catgut, but does not state the method by which it was prepared, while Webber reports three cases following iodized catgut. For septic cases an absorbable ligature has such undoubted advantages, in that the suppuration is not maintained by the presence of a foreign body, that, if reasonable certainty of disinfection can be obtained, this material should be used. In aseptic cases there seems to be no objection to the use of silk or thread. Many surgeons use catgut for all purposes.

LOTIONS

Lotions of great variety are in common use by most surgeons during their operations. Between the "aseptic" school, who avoid lotions or use only sterilized water or saline solution, and the "antiseptic" school, who use strong germicides freely, there lies the great body of general surgeons who rely chiefly upon complete sterilization but prefer at the same time to use antiseptic lotions sparingly during their work.

A very large number of chemical substances have been introduced into surgical practice in the effort to secure the ideal antiseptic, which shall at the same time be reliably and actively germicidal, non-toxic, non-irritating, penetrating, and sufficiently non-volatile to ensure prolonged action. It should also be a stable compound, even when it is introduced into the tissues, should not combine with albumin, *should be freely soluble, and should not stain the skin*, clothing, or instruments.

Biniodide of mercury in watery solution, and alcohol, are, we believe, the most suitable antiseptics for general operative work. Many other substances, however, such as hydrogen peroxide, *iodine*, *carbolic acid*, lysol, and formalin, hold valuable places in surgical technique.

Biniodide of mercury or *potassio-mercuric iodide*, perhaps better even than alcohol, fulfils the essentials of an ideal antiseptic. Its toxicity is small as compared with corrosive sublimate or carbolic. It is a powerful germicide, and as its interaction with albumin is very small, its antiseptic value in the tissues corresponds much more closely to its test-tube efficiency than is the case with corrosive sublimate and many of the other mercurial lotions. Its power of penetration is therefore greater than that of corrosive sublimate, and it is comparatively non-irritating. Skins which are very sensitive to carbolic acid, lysol, or other coal-tar derivatives, or to corrosive sublimate, will usually tolerate free and prolonged use of biniodide of mercury without irritation. It stains neither the skin nor linen, nor does it discolour or corrode steel instruments, unless they have been left in

it for some time. The watery solution is more efficient in the tissues as an antiseptic than the more costly alcoholic solution.

Alcohol affords a most valuable method of sterilizing the hands, "far surpassing that of all other agents" (Leedham-Green). The experiments of various observers have shown that the best germicidal value has been obtained with 70-per-cent. dilution of the spirit, used from 4 to 5 minutes. Absolute alcohol is less germicidal than this weaker solution; the alcohol apparently acts not only as a strong disinfectant, but also by hardening the surface of the epithelium and imprisoning bacteria situated in the deeper layers of the skin. It is essential that it be used on the dry hands, otherwise the hardening object is not attained. This is a specially suitable method, therefore, for hand sterilization if dry rubber gloves are to be worn afterwards.

This combination of alcoholic sterilization and epithelial hardening with preservation of the dryness of the hands not only secures an efficient degree of manual asepsis at the beginning of the operation, but tends to maintain it throughout, by avoiding the subsequent softening of the alcohol-hardened epidermis and escape of organisms from the deeper layers of the skin.

Corrosive sublimate, perchloride of mercury, is commonly regarded as an efficient antiseptic, but we believe that its use should be largely abandoned in favour of biniodide. It is very irritating to the tissues and to many skins, has toxic properties, immediately discolours steel and silver instruments, combines strongly with albumin, and is decomposed by soaps and alkalis.

Sal-alembroth, ammonio-mercuric chloride, in its irritating qualities and its power of combining with albumin, occupies a position intermediate between corrosive sublimate and biniodide.

Carbolic acid.—The results of experimental research into the bactericidal power of carbolic acid have been extraordinarily varied, and probably its germicidal action has been very greatly exaggerated. Undoubtedly, however, it has a strong inhibitory effect on the ordinary organisms of disease, even in very dilute solution; thus a solution of 1:800 will cause permanent attenuation of anthrax bacilli grown in it (Pearson). It has been extensively used in surgery since it was first introduced by Lister, but it must be remembered that even solutions of 1:20 are incapable of completely sterilizing either instruments or skin, even if their action be prolonged for several hours. Weak solutions are, nevertheless, quite suitable for preserving the sterility of instruments which have already been sterilized, for not only have they a strong inhibitory action on bacteria, but they neither discolour nor corrode the instruments, nor cause them to be slippery. Carbolic acid is strongly toxic, and, if used freely on large wounds or in extensive cavities, may be absorbed and cause grave constitutional

symptoms. The patient begins by passing a greenish or brownish urine, and later becomes pallid, with small rapid pulse, dilated pupils, blue lips, shallow rapid breathing, and a subnormal temperature. This general depression of the vital centres may pass into a low delirium, and thence into coma and death. Locally, also, carbolic acid has strong toxic effects. It irritates many skins, and if it be applied as a moist dressing (especially if weak solutions such as 1:60 or 1:80 be used) to a part with a "terminal" circulation, gangrene is apt to occur insidiously, the patient being unaware of any morbid sensation owing to the anæsthetic action of the solution. Numerous fingers have been lost in this way.

Creolin (1 to 2 per cent), *cyllin* (purified creolin), *lysol* (1 to 2 per cent.), *microl* (1 to 2 per cent.), *izal* (½ per cent.), are all derivatives of coal-tar.

Lysol, being prepared by saponification of coal-tar oil with alkalis, may be used for its soapy as well as for its antiseptic action. These preparations are all more or less irritating to sensitive skins; they are, however, less toxic than carbolic acid.

Creolin should be mixed with cold water first, for if hot water be added directly to the undiluted creolin, some of the oils are precipitated.

Lysoform is a combination of formaldehyde with soap, which may be used in solutions of from 1 to 5 per cent. It is comparatively non-irritating and non-toxic, and a fairly efficient germicide.

Formalin, a 40-per-cent. watery solution of formaldehyde, is frequently used in strengths of from 1 to 10 per cent. of the formalin, especially for spraying rooms and for disinfecting very septic wounds. Its pungent, irritating vapour is, however, a great drawback.

Hydrogen peroxide (H_2O_2) is a very valuable preparation, especially for suppurating cavities, fistulæ, and lesions infected with anaerobic organisms. When mixed with pus, etc., it causes a free effervescence due to the setting free of nascent oxygen The B.P. preparation should give off 10 volumes of oxygen on decomposition. If used in this strength, however, for comparatively recent wounds, hydrogen peroxide is apt to cause a stinging, unpleasant sensation. It is, however, frequently used in strengths of from 4 to 7 volumes. If it be employed for suppurating cavities, such as the knee-joint, one must remember that it distends the cavity and opens up the outlying pockets of the synovial membrane. If these be infected this is, of course, a desirable action, but if it seems probable that they have escaped infection the hydrogen peroxide may cause its extension from the general joint-cavity into these bursæ, etc. Hydrogen peroxide has the additional advantage that it assists in hæmostasis and in the loosening of gauze plugs. After frothing has ceased, the

wound should be washed clean with some other lotion, to remove débris and disorganized H_2O_2, which, having parted with oxygen, is now little more than dirty water.

Boric acid is a feeble and ineffective germicide, but is of value for its non-irritating and non-toxic effects. It is chiefly used for the irrigation of the conjunctiva and of the mucous membranes, and for the preparation of hot fomentations.

Potassium permanganate possesses, on account of its oxidizing power, antiseptic properties, but unless in strength greater than 5 per cent.—i.e. much more concentrated than that usually employed —it is quite useless. Saturated solutions are used, followed by saturated solutions of oxalic acid, in Schatz's method of preparing the hands for operation.

Tinct. benzoini co. (Friar's balsam) is frequently of value as an immediate application in cases of accidental wounds, and is sometimes used for swabbing out septic cavities, and also in mouth operations (Pearson).

Iodine is a very valuable and powerful antiseptic, which may be used either in the form of the tincture (2½ per cent.), of a diluted tincture in which it is dissolved in potassium iodide (1.5 per cent.), or as a chloroform or ethylene-dichloride solution. If it be used for skin preparation, previous soap and-water treatment should be omitted, for reasons already stated (*see* p. 291). In factories, where wounds are not uncommon, it should be kept in stock for immediate application If this be done, it should be remembered that the tincture, and other potassium iodide solutions, should not be more than one month old; the chloroform solution appears to be much more stable, and therefore more suitable for this purpose. The combination of stimulant with antiseptic properties possessed by the tincture renders it specially valuable in the treatment of chronic fistulæ and sores It actively promotes phagocytosis, and also stimulates the growth of granulation tissue. Its power of penetration through the skin can be increased by cataphoresis

Iodoform.—Although *in vitro* a relatively poor antiseptic, in the tissues iodoform exercises an inhibitive power over microbial growth. Its use had greatly declined before the War, and the value of various emulsions, such as those in glycerine, paraffin or petrol, was regarded as largely due to the excipient used; but during the War its use was greatly revived in the form of B.I.P.P. (bismuth (2 parts)-iodoform (1 part)-paraffin paste). This paste, if not used in excess, proved valuable, if thoroughly applied to all the interstices of a wound which had been previously cleansed with spirit and dried; it often paved the way for delayed primary or for secondary suture. It had the advantage that a wound treated with it required less frequent attention

than one cleaned by the Carrel-Dakin method; but it had several disadvantages, e.g. being impervious to X-rays, it reduced the value of subsequent radiograms; and cases of poisoning were seen with symptoms referable *sometimes to the bismuth content*, sometimes to the iodoform, and sometimes to both. The general symptoms of iodoform poisoning include anorexia, constant taste and smell of iodoform, nervous depression and melancholia, sometimes alternating with periods of hallucination and delirium; there may be pyrexia, yellowness of skin and conjunctivæ, and skin eruptions, and the patient may die in a state of coma. Locally, iodoform may cause an acute dermatitis which may resemble erysipelas.

Paraffin.—Sterilized liquid paraffin can be used to dress granulating wounds, and is very useful in that it prevents the dressing from sticking to the granulations and the growing skin margin, so that no damage is done when the dressing is changed; whether the satisfactory results obtained with it are to be associated with any other property is not quite clear.

Dakin's solution is a carefully prepared hypochlorite solution, especially valuable in treatment of wounds by the Carrel-instillation method (p. 282). This solution, like eusol, which also is a hypochlorite preparation, is of value in rapidly cleaning sloughy ulcers. They must both be carefully prepared, or they will cause much local irritation

Flavine is an aniline dye, is not irritating to the tissues, and is generally used as a 1 : 1,000 solution. It rapidly cleans a wound, but its use should not be continued for more than three or four days, because it also prevents granulation-formation and so delays *healing*. As a preliminary to delayed primary suture it is excellent.

Picric acid in 3-per-cent. solution in spirit is valuable for preparation of the skin before operation. It is less irritant than iodine.

Normal saline solution is a solution of common salt in sterilized water in the strength of 0·65, or, roughly, 1 drachm to the pint. It approximates in specific gravity to blood-plasma, and therefore, on *account of its non-irritating* and non-devitalizing characters, if prepared under aseptic precautions, affords an excellent lotion for all fresh wounds, for skin-grafts, and for delicate membranes such as the peritoneum.

Sterilized water is freely used by many surgeons, and may be prepared by boiling water for five minutes in Florence flasks, which are then corked with sterile cotton-wool and allowed to cool.

PRINCIPLES OF OPERATIVE PROCEDURE

Although the general principles of operative procedure cannot be discussed in detail, we must emphasize the necessity for the avoidance of all scratching with the knife or raising of the *skin from* the

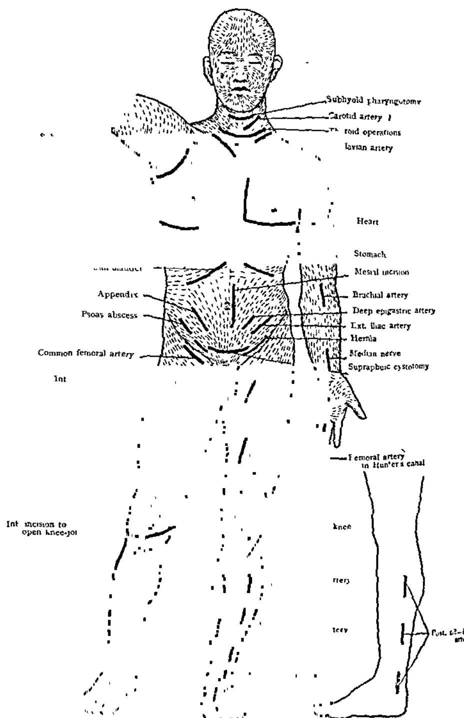


Fig. 12.—Incisions determined by lines of stress, as shown in Langer's figures.

(From Kocher's "Operationslehre")

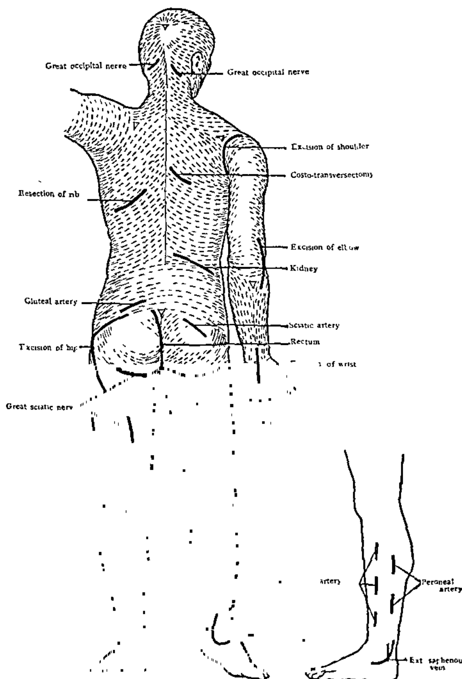


Fig 14.—Incisions determined by lines of stress, as shown in Langer's figures.
(From Kocher's "Operationslehre")

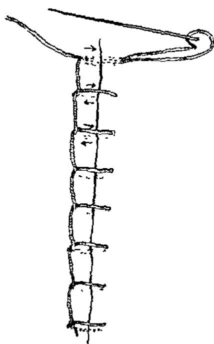


Fig. 21.—"Blanket" suture.

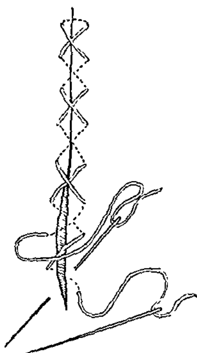


Fig. 22.—Crossed continuous or "bootlace" suture.

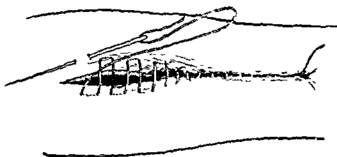


Fig. 23.—Cushing's right-angled continuous suture.

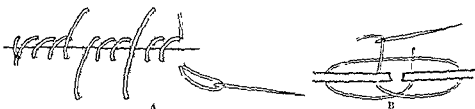


Fig. 24.—Continuous suture combining coaptation and relaxation (tension) stitches.

A, The suture seen from outside B, Sectional view

of invagination, such as the purse-string (Fig. 25), the Lembert (Fig. 26), and others used in intestinal, urinary, and vascular surgery. For



Fig. 25.—Purse-string suture.

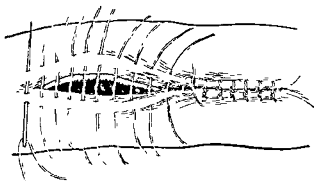


Fig. 26.—Lembert's invaginating suture.

further information the reader must be referred to textbooks on Operative Surgery.

Metal clamps.—A valuable method of skin coaptation is afforded by Michel's and similar metal clamps (Fig. 27) They can be boiled without detriment, and, being purely cuticular in their application, they do not form a track from the surface to the deeper layers of the wound; while, if removed sufficiently early, they leave none of

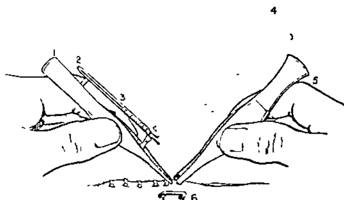


Fig. 27.—Michel's suture clamps.

1, Nibbed forceps to which is attached the spring clip, 2, spring clip for holding clamps ready for use, 3, clamps, 4 and 5, forceps with broad groove at points, in which is held the clamp, the clamp is applied by sharply flexing it by pressing blades of forceps together, 6, a clamp before flexation

the suture marks which are the chief cause of unsightliness in the ordinary scar. It is necessary to warn the surgeon that unless he remove the clamps by the fifth or sixth day he will be confronted

with small pressure ulcers which may leave scars as unsightly as stitch marks.

Another variety of metal clip is that of von Herff (*serres fines*), which has the advantages that it is applied and removed by the surgeon's fingers and that it can be re-sterilized and used repeatedly (Fig. 28).

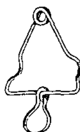


Fig. 28.—Von Herff's clip.

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BURNS AND SCALDS

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AND

HAMILTON DRUMMOND, B.S., F.R.C.S.ED.

Definition.—A burn results from the action of dry heat upon the tissues, whereas a scald is produced by the application of moist heat. The former is comparable to roasting and the latter to boiling. The effects upon the tissues and the body generally are, however, so essentially similar that one description will apply to both. Special mention will be made of scalds of the throat, a very fatal condition requiring special treatment.

In the statutes of Great Britain the injuries produced by such corrosive liquids as sulphuric acid, nitric acid, caustic potash, etc., are considered as burns, and, indeed, the pathological and clinical features show a great similarity to those of injuries produced by heat.

Mortality.—Burns are responsible for a great number of deaths every year, and contribute a large percentage of the fatal cases in any large hospital in a manufacturing town. Thus, in a recent year 63 cases of burns were admitted to the wards of the General Hospital, Birmingham; of these 34 ended in death, making a mortality of nearly 54 per cent. In the same period 16 cases of scalding were admitted, with a mortality of 25 per cent.

It would appear that the percentage of deaths from burns in females is greater than that in males, especially in the case of those over 5 years of age.

Inasmuch as the majority of burns in children are caused by ignition of the clothing, due to playing with matches or with the fire, the greater number of such accidents occur in the colder months of the year. Adult males are generally burnt or scalded at their work, by gas or boiler explosions, or by contact with molten metals; whereas, in the case of women and of children, it is usually some article of clothing that catches fire.

Classification.—Many different classifications have been adopted from time to time. American and German writers usually consider burns in three degrees. In France and in this country Dupuytren's

method of classification in six degrees, according to depth, is usually adopted, and will be followed here.

The *first degree* is characterized by an erythema of the skin of quite a superficial and evanescent nature.

The *second degree* is associated with the formation of vesicles filled with serum, the epidermis being raised from the skin by the cutaneous inflammation.

In the *third degree*, part of the thickness of the papillary layer of the skin is destroyed.

The *fourth degree* indicates complete destruction and disorganization of the dermis down to the subcutaneous cellular tissue.

In the *fifth degree* there is a charring of all the superficial soft parts, including more or less muscle, down towards the bone.

The *sixth degree* is characterized by complete carbonization of the burnt part.

Most cases present several different degrees combined, but a burn is classified according to its most severely damaged portion. It is frequently noticed that a burn which at first appears to be of the third degree, eventually turns out to be also partly of the fourth.

Clinical aspects. Local effects.—In burns of the *first degree* the skin is merely scorched and there is no destruction of tissue. There is a dilatation of the blood-vessels, causing redness; the part is painful and often somewhat œdematous. After some hours, or at most a day or two, there is a return to normal, with a little superficial desquamation of the epidermis.

In the *second degree*, in addition to the hyperæmia of the burnt part, there are blisters, containing, as a rule, a clear yellowish serum. When these are opened the papillary layer of the skin is exposed beneath the raised epidermis in bright-red patches, which are acutely tender. Healing, however, is rapid and without scarring, though some pigmentation may remain.

In the *third degree* the epidermis and papillary layer of the skin are transformed by heat into dull-yellowish or brown patches, insensitive to light touch. The pain, though considerable at first, soon passes off, only to return again, to some extent, a few days later, when the reaction has become established

Healing is by granulation, but the spread of young epithelium is rapid, since it not only grows in from the edges, but also arises as isolated islands among the granulations, from the epithelial remains of skin which have escaped destruction. A dull-white scar results, and since the formation of granulation tissue is not excessive, little contraction or deformity is to be apprehended.

Burns of the *fourth degree* are the most important with which we have to deal. The whole thickness of the true skin is destroyed, the

destructive process being often shared to a greater or less extent by the subcutaneous connective tissue and fat.

Dry yellow or yellowish-black insensitive eschars are formed, surrounded by a red zone of congestion. This line of redness, it may be noted, is a sign of vital reaction, somewhat analogous to the line of demarcation between living and dead tissue seen in gangrene. It is visible very soon after the burn is inflicted, and in fatal cases may be taken as a sign that the burn was inflicted during life. Christison found that it was impossible to produce this line in bodies that had been dead ten minutes.

Owing to the fact that the nerve terminals are destroyed with the skin, the pain that is felt is mostly experienced in the surrounding parts that have not been burnt to the same depth. Suppuration to a greater or less extent almost invariably follows burns of this degree, and when the sloughs separate, large cavities are left which fill with granulations Since the glands in the skin are destroyed, the spread of new epithelium is limited to that which can take place from the margins of the ulcer, a process which is an extremely slow one where there are large raw surfaces. There is often a very free growth of granulations, which require treatment.

In such circumstances the formation of scar tissue is excessive, and its contraction is liable to lead to much disability and deformity. Cheloid frequently develops in such scars (Fig. 29), and, when the face is affected, unsightly deformities may result, such as ectropion, and distortion of the mouth and ears. Joints may be flexed, and the fingers rendered useless by being twisted into shapeless appendages, as in the case illustrated in Fig. 30. The upper arm may even become united to the side of the chest in extensive burns of the arm and trunk.

Burns of the *fifth* and *sixth degrees*, if not rapidly fatal, are usually of limited extent, being confined, perhaps, to one of the limbs. They are caused by prolonged contact with heated metal or by the action of caustics or the burning of phosphorus.

General effects.—The after-effects of burns and scalds upon the body generally have been divided into three stages :—

1. Shock and collapse.
2. Inflammation.
3. Suppuration and sepsis.

The *stage of shock* usually lasts from twenty-four to forty-eight hours, and varies in severity with the superficial area of the body involved, the degree of the burn, and the age of the patient. Shock is commonly most profound in infants, though pain is often not marked, even in the gravest cases. The usual phenomena of shock are present : the pulse is rapid, and frequently imperceptible at the wrist ;

the temperature is lowered, and often to such a degree that the clinical thermometer is unable to register the fall; the *surface of the body* is



Fig. 29.—Development of cheloid upon the face of a girl, in the scar of a burn.

(*Photograph by Dr. Emrys-Jones.*)

cold and covered with sweat; thirst is extreme, and the child constantly cries out for something to drink.

As reaction comes on, the second stage is entered upon, the *stage of inflammation*, which may be said to last until the sloughs are separated,



Fig. 30.—Marked deformity of thumb caused by cicatrization after a burn.

(*Photograph by Dr Emrys Jones*)

in from one to two weeks. The temperature rises to 102° F., or even 104° F., the rise being associated with definite reaction in the internal organs, such as broncho-pneumonia and bronchitis, especially when the thorax itself is burnt. It is alleged that inflammation of the

various parts of the intestinal tract is peculiarly liable to follow burns on the abdomen. Duodenal ulcer, with perforation, was formerly said to be a common complication of burns, but this statement is open to some doubt. Certainly in these days, when everyone is familiar with the symptoms presented by perforating ulcers of the duodenum, one does not see or hear of cases occurring as a result of burns.

In an experience of over 200 cases of severe burns, only in one case was melæna noted. In that case there were no symptoms pointing to the seat of the hæmorrhage, so that it may have come from almost any part of the intestinal tract; the patient recovered. Albuminuria is common, and this may be associated with degenerative changes in the kidneys.

The third stage, the *stage of suppuration*, lasts from the end of the second period until the wound is healed. Its duration, therefore, is very variable, and may be protracted for months. The complications of this stage are mostly the result of long-continued suppuration and sepsis, and can, therefore, be controlled to a considerable extent by skilful treatment conducted on modern surgical lines.

Pathology and modes of death.—As the result of a fire in a building, persons may be suffocated, and death occur from poisoning by carbon dioxide or carbon monoxide; in the latter case the characteristic cherry-red colour of the blood, produced by carbon monoxide hæmoglobin, will be observed. The largest number of deaths occur during the period of *shock* Out of 207 fatal cases of burns and scalds no fewer than 128 died from shock either on the same day or on the day following the injury. The intensity of the shock depends far more on the superficial extent of the burn than on its depth. Burns involving one-half of the body are always fatal, and those affecting one-third nearly always end in death. Children frequently die when the front of the chest and abdomen is burnt to the second degree, the greater part of the burnt area being only of the first degree. Cases are recorded of adult males dying from shock when extensively burnt to the first degree only. Burns over the great serous cavities are more dangerous than those on the limbs.

Many theories have been advanced to explain the fatal issue during this period. It was formerly suggested that the extensive interference with the various physiological functions of the skin was sufficient to cause rapid death. The pathological changes in the body fall under three heads: those due (1) to shock, (2) to non-bacterial toxins, and (3) to septic infection. The symptoms produced by each factor merge into the others, and it is impossible clinically to draw any hard-and-fast line of distinction between them. Shock consists in a state of profound depression of a large number of centres in the grey matter of the central nervous axis. The source of the afferent impulses

productive of this state of central inhibition is the widespread and serious damage done to multitudes of nerve-endings in the skin and underlying structures. The histological accompaniment of this nerve exhaustion is evidenced by a certain degree of chromatolysis, or partial destruction of the granules of Nissl. Degenerative changes in the internal organs, especially the liver, kidneys, and lymph-glands, similar to those produced by the bacterial toxins of typhoid and diphtheria, have been observed by Bardeen and McCrae before sufficient time had elapsed for septic infection to occur. Cloudy swelling has been noted within six hours of the occurrence of a burn. The toxins responsible for these changes are produced by the physico-chemical damage to the tissues of the skin and proteins of the blood as a result of the application of heat. At the same time, it is to be remarked that experiments upon animals have not confirmed the presence of specific toxins in the blood and tissues from cases of burns.

During the stage of inflammation, congestion is liable to appear in the lungs and pleura, the intestines, the brain and its meninges; and in the event of marked infection the usual signs of severe septic intoxication are observed in the internal organs. *Toxæmia* ranks second to shock as a cause of death following burns, and is produced by toxins both bacterial and non-bacterial in character. Pyæmia is a rare complication, as is shown by the fact that in a series of over 200 cases I (C. W.) have seen only one instance of this condition. Infection with extraneous pathogenetic bacteria may occur, as in any other open wound, and one case of tetanus following a burn was recorded in Birmingham in 1903.

Treatment. General.—The majority of patients, when first seen, are in a state of profound shock urgently calling for treatment. Every effort must be made to get the patient warm and to restore the failing circulation. As a substitute for the somewhat inefficient hot-water bottle, the device employed by Waterhouse is useful. In the case of a child, a 32-candle-power electric lamp is placed beneath the cradle which covers it, and the temperature of the air can thus easily be maintained at about 103° F. until shock has passed off. Normal saline solution should be slowly injected into the rectum every few hours in quantities varying from 2 oz. for a small child to a pint for an adult. Half an ounce of brandy may be conveniently added to the saline, especially when it is difficult to administer anything by the mouth. Brandy is probably the most useful stimulant in these cases, and should be given freely. When shock has set in severely and the blood-pressure is much lowered, perhaps the best method of restoration is by an intravenous injection of 6-per-cent. gum saline solution. The solution should be injected into the cir-

culation slowly at the rate of fifteen minutes for each pint; as a rule, a pint is sufficient.

It is doubtful whether any good effect follows the use of the commercial preparations of pituitary extract, even when given intravenously. Such cardiac stimulants as digitalin, strophanthin, and strychnine have been recommended, but they are of as little use here as in the treatment of shock produced in other ways. When fluids can be taken by the mouth, often-repeated small drinks of warm water should be given; after a few hours, milk may be added to the water.

One of the most difficult questions to decide is the propriety of administering morphia. Adults suffering from severe burns bear this drug well, but with children the greatest caution must be exercised. To children obviously doomed from the first, it is permissible to give an opiate to afford some degree of relief from suffering; but in other cases, in which the patients are not so extremely burnt, or in which the prognosis is doubtful, morphia should most certainly be withheld if possible.

Local.—The condition of a burnt part is one in every way favourable to the development of sepsis. The surgeon's endeavours should therefore be directed towards preventing the growth of septic organisms, and securing as aseptic a condition of the skin as possible.

It is important that the strictest antiseptic measures should be carried out without loss of time. The burnt parts should be carefully washed with some antiseptic lotion of a mild character and some form of ambrein wax applied, either with a brush or by means of a spray. Care should be taken to prevent mixture of water with the wax, as the latter alone will not burn the tissues at 176° C., but it melts at 52° C., and a drop of water present will cause scalding. The object of employing the spray is to cover the burnt area with a non-adhering layer of wax, which can easily be removed.

The wax should first be sterilized by placing it in a spray and heating on a spirit lamp or burner to 120° C. The flame should be allowed to play on the nozzle of the spray for a short while in order to prevent solidification of the wax in the tube.

The whole of the affected area should be sprayed until it assumes a covering of waxy globules not unlike a hoar-frost. Further applications of the spray should be made to the area until the whole field is covered by a solid layer. A portion of dry gauze is then applied to the surface of the waxed wound, and the whole is painted over with melted wax with the aid of a brush. Whether the spray method or the brush is employed, it is essential to have the area perfectly dry before the wax is applied.

Lieutenant-Colonel A. J. Hull finds the following application and formula to give the best results:—

The burnt area is first washed with 1-in-1,000 aqueous flavine solution, then dried with gauze or an electric drier, and covered with No 7 paraffin. No. 7 paraffin is made thus: To 678 grm. of hard paraffin, melted, 210 grm. of vaseline and 50 c.c. of olive oil and 2½ grm. of β-naphthol are added.

The temperature of the mixture is allowed to sink to 55° C., and 20 c c. of eucalyptus oil is added; it is then stirred and allowed to solidify.

A layer of the paraffin mixture is now applied at a temperature of about 55° or 60° C., and covered by a thin layer of wool, another layer of paraffin is applied, and a wool and bandage dressing complete the procedure. The wound is dressed every twenty-four hours, and another dressing of the same kind is applied. If the paraffin is applied too hot, the layer is too thin, and will not peel off in a sheet.

Burns up to the third stage can be safely treated, and do best, by the wax treatment. This treatment has several points in its favour. It is easily applied, and the wax forms a firm hard dressing completely resting the damaged tissues. It is easily removed without pain to the patient, and it does not interfere with the growth of new epithelium. It should not, however, be employed in very septic cases, unless the areas are but small

If stronger antiseptics, such as carbolic acid or corrosive sublimate, be employed, the parts should afterwards be well washed in normal saline solution. To carry out this preliminary cleansing satisfactorily it is often necessary to give a general anæsthetic. All blisters must be snipped away, since their contents are found to be invariably infected with micro-organisms, and, unless they are laid open, the antiseptic cannot gain proper access to the interior.

The most satisfactory solution to employ as a primary first aid dressing is one containing picric acid. The formula usually given is: Picric acid 1½ dr., absolute alcohol 3 oz., distilled water 40 oz. Gauze or lint should be lightly wrung out of this solution and applied all over the burnt areas, which are then covered with antiseptic wool and bandaged. A point to be insisted on is that no waterproof covering of any kind should be used. The dressing of burns with poultices or any form of fomentation is a pernicious practice. Dryness of the dressings should be aimed at, for this hinders the rapid multiplication of organisms and prevents the dressings from being so soon soaked with discharge, and thus obviates the necessity for frequently changing the dressings, a process always painful to the patient.

Picric acid seems, in some cases at any rate, to have a fairly marked action in relieving pain. It possesses also the property of encouraging and assisting the growth of young epithelium, and for this reason it should not only be used as a first dressing, but should be continued well

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on to the commencement of the third stage. It is alleged that the use of picric acid as a burn dressing is frequently followed by poisoning, manifested by such symptoms as vomiting, diarrhœa, dark-coloured urine, yellow vision, and coma. In several hundred cases under my (C. W.'s) observation treated with picric acid no evil effects have been observed to follow its use. We owe the introduction of the picric-acid method to the writings of Thiery and other French surgeons. This substance is conveniently employed for burns of the first and second degrees, but its principal use is for those of the third and fourth degrees.

It is nowadays hardly necessary to mention that carron oil, or any preparation containing oil or grease, should find no place as a primary dressing in the treatment of burns or scalds. The use of oil combined with antiseptics, such as carbolic oil, defeats its own object, for the oil prevents ready ionization of the antiseptic; and it is upon *the power of free ionization that its germicidal action depends.* Moreover, carbolic oil is a fruitful source of carboluria, though it does not apparently produce carbolic gangrene.

Formerly iodoform was largely used, but there is no little danger of the production of symptoms of poisoning when it is applied to extensive areas.

The method of treating burns by continuous immersion in a warm bath has much to recommend it, though in practice it is not always easy to carry out. Where only the limbs are burnt it is, of course, much more conveniently used, and is very satisfactory.

After the sloughs have separated, large and usually septic ulcers remain for treatment. The surgeon's ingenuity is often taxed to find an application suitable for a particular case; a change of dressing will often prove beneficial. Among recent preparations, sorbefacin has *proved of considerable service in many cases; it seems to have a favourable influence in promoting the growth of epithelium.* Boric ointment is best used at a half or quarter the strength of the Pharmacopœial preparation, as in the usual strength it often produces a papular eruption. Both boro-glyceride and zinc ointments have their place, the latter being often conveniently combined with equal parts of castor oil.

Ointments containing balsam of Peru or tinct. benzoinæ co. or amido-azo-toluol (4–8 per cent.) (the active principle of scarlet-red) are of service when a stimulating application is required. As a non-irritating, non-toxic, but fairly powerful germicide, a 1-per-cent. solution of aluminium acetate is extremely useful. Some even use it as a primary dressing in burns, to the exclusion of picric acid.

Exuberant and redundant granulations must be kept in check by the use of caustics, and sometimes by free scraping under an anæsthetic.

Wherever possible, the large ulcers arising from burns should be skin-grafted after the method of Thiersch (*see* Vol. III.).

Care should be taken, by the timely use of splints, to prevent the occurrence of those deformities of the limbs which are so apt to result from contracting scars. At a later stage, various plastic operations have to be planned for dealing with flexed limbs and other deformities that may have been produced. Amongst other complications which occasionally arise may be mentioned secondary hæmorrhage; this may take place from a large vessel in very deep burns, or, more commonly, from superficial veins during the separation of sloughs in burns of the fourth degree. Hæmorrhage from superficial veins occurs in about 2 per cent. of burns; and it is usually the upper extremity that is affected. We have never seen it in children. When it is met with it is to be treated by the usual hæmostatic measures. Tetanus is a much rarer complication than was formerly the case, and is to be treated on the usual lines (p. 927 *et seq.*).

Children suffering from burns not infrequently present certain symptoms, including a scarlatiniform rash, which sometimes occasion anxiety, especially if cases of scarlet fever are numerous in the neighbourhood. The question of isolation naturally arises; but, as a rule, the rash is merely a toxic one. Still, it is wise to err on the side of safety and to isolate in any doubtful case.

SCALDS OF THE PHARYNX

These cases usually occur in infants and young children through the swallowing of hot fluids. It is not the injury received by the mucous membrane of the mouth and tongue that causes much apprehension, but the œdema of the upper aperture of the larynx which always, to a greater or less degree, follows such injury. On this account a child with a history of a recent scald of the mouth should be kept under close observation. Otherwise, though apparently but little injured when first seen, he may be brought back to the surgeon in the small hours of the night dying of suffocation and requiring imme- [illegible] l of the [illegible] examination of the upper aperture of the larynx with the finger will reveal the great swelling of the aryteno-epiglottidean folds. The epiglottis also shares in the œdema, but not usually in any great degree. The milder degrees of the œdematous swelling can be treated by scarification, the use of a steam tent, and doses of antimony wine. Frequently, however, the time at which these milder measures would have been serviceable has already passed when the surgeon sees the child.

As the œdema of the glottis increases and still further hinders the

entrance of air into the trachea, the breathing becomes more and more laboured, as is evidenced by intercostal and suprasternal indrawing and by increasing cyanosis.

If the windpipe has to be opened, high tracheotomy or intercrico-thyrotomy is the most suitable operation. The mortality after tracheotomy in such cases is very high, and it is therefore well to employ intubation whenever possible. This method has many advantages. It may be used in much earlier stages, when one is doubtful as to how far the œdema will go and when tracheotomy would therefore be unjustifiable. Being used early, it keeps the air-passage free, and thus avoids several hours, perhaps, of laboured and increasingly difficult respiration, exhausting the patient and tiring out the heart, which will presently be taxed to its uttermost during the stage of acute inflammation in the bronchi and bronchioles that so often follows. As a cutting operation is avoided, the patient escapes the added danger of blood getting into the air-passages. Of course, intubation implies the necessity for skilled assistance being always within a moment's call, such as is usually only obtainable in hospital.

After the danger of suffocation has been overcome, the patient still has to run the risk of acute capillary bronchitis and broncho-pneumonia, which may prove fatal from heart-failure.

ELECTRIC BURNS AND SHOCKS

Under this heading are considered those injuries which are produced by lightning and by powerful electric currents. Burns from lightning and electricity may be classified in the same manner as those caused by fire. There are, however, certain absolute differences between electric and ordinary burns, in that, according to Mally, the former are painless, dry, aseptic, and usually more or less round *in shape, while the reaction of the tissues is extremely slow.* These characters are due to the rapidity with which the injuries are produced, the high temperature associated with an electric discharge, and the small total amount of heat involved in the process.

The results of a **lightning-stroke** may be manifold, and vary in the most extraordinary manner. One person may have his clothes stripped from off his back, or may be killed and mutilated, whilst a friend standing next to him escapes without suffering the slightest inconvenience The lesions occasioned by lightning include wounds of almost every description, fractures which may be simple or compound, and burns of varying shape and depth. As far as the burns are concerned, there is a peculiar condition occasionally seen, known as arborescent markings, which requires mention. Delicate-branching, almost fern-like patterns are seen. They do not follow the lines of lymphatics or superficial blood-vessels, as was at one time suggested.

In addition to these lesions, various subjective phenomena are sometimes observed, such as blindness, deafness, various paralyses, loss of memory, etc. The burns produced may at times be noted to take the form of metallic objects carried on the person, the objects themselves being often fused. In this connexion it may be observed that if certain metallic articles, such as knives, carried by a person found dead, are on investigation discovered to be magnetized, a clue



Fig. 31.—Electric burn caused by falling on a live rail.
Note the great depth of burn in centre of wound

is at once given to the cause of death, should this at first sight not be obvious

It was formerly asserted that rigor mortis did not usually occur, but it is now known that it does so invariably, the explanation being that often it both appears and disappears very quickly and is, therefore, perhaps not present when the body is first found. Putrefaction sets in early.

The injuries produced by powerful **electric currents** possess several peculiarities requiring mention. The lesions are most evident at the points of exit and entrance. The superficial degrees are painless and aseptic, while healing is very slow. In the severer degrees there is much shock; and pain, practically absent during the first twenty-four to thirty-six hours, later becomes very severe. A form

of slow, moist gangrene sets in, and the *sloughing* process tends to spread.

Since these burns are often *deep* (*Fig. 31*), sloughing is likely to be associated with secondary *hæmorrhage* from large vessels. Besides the local injuries, there are to be observed signs of shock, with extreme pallor, stertorous breathing, and *insensibility*.

The **treatment** of *injuries* produced by lightning or electrical currents consists in combating *shock* and keeping the burnt parts aseptic. The complications are treated on *general principles*. When shock is overcome the prognosis is usually good. As a rule, the paralyses mentioned above *eventually* disappear, but complete restoration may be slow.

In the *case of* electric currents the cause of death may be heart-failure or paralysis of the respiratory centres, depending on the kind *of current* involved. Respiratory paralysis is brought about by the *action on* the medulla of very high-tension currents, both direct and *alternating*, and may be successfully treated by artificial respiration, kept up, if need be, for hours, provided the heart's action be not *impaired*. Heart-failure results from lower voltage shocks, and is more likely to be caused by alternating currents of low than of high frequency. The musculature of the heart ceases to beat rhythmically, and is thrown into a state of fibrillary contraction. Once established, this condition always proves fatal, as no means have been devised for successfully combating it; though, experimentally, Prévost and Batelli restored the normal rhythm to a heart in fibrillation by applying to it a high-tension current before the blood-pressure had fallen to zero.

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CONSTITUTIONAL DISTURBANCES ASSOCIATED WITH TRAUMA

By RUSSELL HOWARD, C.B.E., M.S., F.R.C.S.

HÆMORRHAGE

Definition and varieties.—Hæmorrhage is the escape of blood from the blood-vessels; and corresponding to the three varieties of blood-vessels there are three varieties of hæmorrhage—*arterial*, *venous*, and *capillary*—each with its own local symptoms and treatment The general symptoms, which depend on the depletion of the tissues of blood, are the same for all varieties of hæmorrhage

Hæmorrhage is also classified into *external*, when the blood escapes entirely from the body and can be seen, *internal*, or *concealed*, when the blood remains in one of the large cavities of the body—e g the peritoneal cavity A third classification of importance is into *primary*, *intermediary*, and *secondary*.

Primary hæmorrhage is the escape of blood from the blood-vessels immediately after the lesion which damages them—i.e. it is immediate, and is the variety of hæmorrhage most often seen and most often requiring treatment.

Intermediary hæmorrhage is said to occur when the bleeding is delayed but does not depend upon infective processes opening up the blood-vessels. It is most often seen after operations accompanied by a severe degree of shock. Hæmorrhage may not occur at the time of wounding of the vessels owing to the low arterial blood-pressure; but as the condition of shock passes off and the blood-pressure rises, the temporary coagula are driven from the blood-vessels and hæmorrhage is started.

Secondary hæmorrhage is caused by ulceration of the wall of a vessel before thrombosis has occurred in it or by digestion of the clot, and it may or may not have been preceded by primary hæmorrhage. The condition is not seen so often as formerly when infective processes followed almost all operations, but it still remains as a most dangerous form of hæmorrhage with peculiar difficulties in its treatment.

Natural arrest of hæmorrhage.—The natural arrest of hæmorrhage is best studied in bleeding occurring from a moderate-sized artery, although the process is essentially similar in veins and capillaries. It can be divided into two stages—*temporary* arrest and *permanent* arrest.

Temporary arrest is brought about by the coagulation of blood forming a plug in the mouth of the cut vessel, but this process is helped by several factors. When an artery is cut across, the middle muscular coat contracts and so diminishes the lumen of the vessel and checks the escape of blood. At the same time, retraction of the middle and the internal coats occurs; this further diminishes the lumen of the vessel, and also establishes contact between the flowing blood and a roughened, non-endothelial surface, and so provokes clotting. The retraction is most pronounced in the internal coat, which, owing to the elastic recoil of Henle's membrane, becomes curled up inside the vessel, and may completely occlude it. This combination of contraction and retraction of the walls of the vessel is sufficient in some cases immediately to arrest hæmorrhage, even from a large artery, such as the popliteal, if it be torn across and not cut.

The change from fibrinogen to fibrin first takes place outside the blood-vessel, forming an external clot and diminishing the flow by mechanical pressure. As the flow becomes progressively less, coagulation occurs in the mouth of the vessel, and gradually invades the lumen, forming an internal clot which effectually arrests the flow. The formation of this clot in the mouth of the vessel is aided not only by the local conditions described above, but also by general conditions which are important and influence the treatment of hæmorrhage. As the blood escapes from the vessels and its total quantity in the body diminishes, there tends to be a fall in the blood-pressure. This tendency to fall is counteracted by increased frequency and force of the heart's beat and by contraction of the blood-vessels generally, so that a large loss of blood can occur without materially affecting the general blood-pressure. But as the loss continues the heart beats less and less forcibly, the blood-vessels dilate, and the blood-pressure begins to fall, with a corresponding diminution in the force and quantity of the flow from the damaged vessel. This change favours coagulation in the vessel and helps to control the hæmorrhage; therefore the larger the quantity of blood lost the greater the tendency to natural arrest. It follows that stimulants which increase the force of the heart's beat and raise the blood-pressure should never be given in cases of hæmorrhage until all the bleeding has been securely stopped.

With the escape of blood from the blood-vessels a second pheno-

menon occurs which also aids the coagulation. The relative number of white corpuscles increases, and there is a flow of lymph from the lymphatic channels into the emptying vascular system. This causes a greater coagulability of the blood, and the change from fibrinogen to fibrin is brought about with great rapidity. Severe hæmorrhage therefore favours its own natural arrest.

A point of importance to be noted here is that whilst retraction of the coats of the vessel helps the natural arrest of hæmorrhage if the vessel be cut completely across, it will hinder it if the vessel be only partly severed. The retraction in this case will cause the wound in the vessel to gape, and thus favour the loss of blood. These lateral wounds, even in small arteries or veins, will often bleed severely, but arrest can frequently be brought about by completely severing the vessel, retraction then tending to check the hæmorrhage.

Permanent arrest.—A wound in an artery heals in exactly the same way as a wound in any other tissue: by the formation of granulation tissue, which joins the cut surfaces together and then gradually changes to fibrous tissue that contracts and finally seals and obliterates the lumen of the blood-vessel. The coagulum takes no part in the final healing of the wound in the vessel, except to form a scaffold on which the granulation tissue is laid down The granulation tissue is formed by a multiplication of the original cells of the part, including the endothelial cells of the vessel, whilst the new capillaries are budded out from the vasa vasorum. The coagulated blood is gradually removed by the phagocytes, and its place taken by the granulation tissue. Fibres of white fibrous tissue are then formed in the granulation tissue and stretch across the gap in the vessel, which thus becomes permanently sealed by a mass of fibrous tissue.

Recovery from hæmorrhage is not, however, coincident with either the temporary or the permanent arrest of the blood-flow, for the general effects have to be considered, and recovery can only be said to occur when the quantity and quality of the blood in the body have been restored to normal.

Shortly after a severe hæmorrhage the specific gravity of the blood is found to be lowered, showing a diminution in the solids in solution and an increase in the water; a leucocytosis is also present, nucleated red blood-corpuscles are seen, and the red cells are diminished in number and in their individual hæmoglobin content. The condition of the blood is that of a secondary anæmia.

In the case of a young subject recovery from this anæmia is rapid, especially if food be freely taken and iron be given; but in an elderly patient it is slow, the blood-forming organs being partially exhausted,

so that in old age a severe hæmorrhage leaves traces in a permanent anæmia and a lessened vitality of all the tissues.

SYMPTOMATOLOGY

The symptoms of hæmorrhage naturally fall into two groups—*general* and *local*. The general symptoms are the same for all varieties of hæmorrhage, and depend upon the amount and the rapidity of the blood loss, while the local symptoms depend upon whether the bleeding is arterial, venous, or capillary, external or concealed, primary or secondary; and the treatment locally varies with local conditions.

General symptoms of hæmorrhage.—As the hæmorrhage proceeds, the patient becomes increasingly pale, the pallor being most easily determined by the colour of the mucous membranes and conjunctivæ. The body is usually covered with sweat; the patient becomes more and more restless, throwing the arms about and moving *in bed; complaints are made of thirst; the* pulse-rate rises *steadily*, and the tension of the pulse falls. Respiration becomes deeper and quicker, and eventually is sighing (air-hunger); the temperature tends to fall below normal, and the extremities become cold. Vomiting is common, and the patient has attacks of syncope, during which he loses consciousness; the pupils become dilated, and dimness of vision or sudden loss of sight (amaurosis) occurs; and there is a singing or buzzing in the ears Finally, the musculature is relaxed, the heart fails, Cheyne-Stokes respiration and unconsciousness supervene, and death follows.

Local symptoms. Primary arterial hæmorrhage.—In the case of a severed artery the blood is bright red in colour, is rapidly lost, and spurts out of the vessel with considerable force in a *series of jerks corresponding to the beats of the heart*; the rate of loss is such that if a large artery—e.g. the common carotid—is severed, death will ensue in less than two minutes. An apparent exception to the intermittent flow of arterial hæmorrhage is seen when an artery is cut at the bottom of a deep, narrow wound. In this case the blood, although arterial, may flow evenly away from the mouth of the lesion, the intermittence being lost in the depth of the wound.

The chief flow takes place from the proximal (heart) end of the *divided artery, but in vessels with a free anastomosis* hæmorrhage from the distal end is often severe and deserving of consideration in treatment; it accounts for some cases of intermediate hæmorrhage, the collateral circulation on being established causing *bleeding from* the unsecured distal end of an artery.

Primary venous hæmorrhage.—In venous hæmorrhage the blood escapes comparatively slowly from the vessels, owing to the low blood-pressure; but the volume, if a large vein such as the internal

jugular be severed, may be considerable. The blood, as a rule, flows evenly and smoothly from the wound and is dark in colour; in venous hæmorrhage from acutely inflamed tissue, however, the colour of the blood is much lighter than usual. Intermittent flow from veins is seen in hæmorrhage from the great veins of the neck and from all the large veins that are influenced by the thoracic movements, especially if the blood comes from a lateral opening in the vein. The intermittency of the flow is not dependent upon the heart's beat, but upon the movements of respiration. On inspiration the negative pressure in the thorax is increased, the venous return is quickened, the veins tend to collapse, and the flow diminishes. It is at this moment that entrance of air into the veins is to be feared. With expiration the negative pressure in the thorax is diminished and may give place to a positive pressure, the veins swell, and the flow from them is increased.

Hæmorrhage chiefly takes place from the distal end of a vein, bleeding from the proximal end being prevented by the valves; but it may be severe from the proximal end in cases of varicose veins where the valves are incompetent, in veins that have no valves, and in those that are markedly influenced by the movements of respiration.

Air in veins.—Air may be sucked into veins by the negative pressure in the thorax, especially if the great veins of the neck are wounded during an operation. This accident can be diagnosed by a curious characteristic sucking noise. If only a small amount of air finds entrance no symptoms follow, but if the quantity is large the heart's action becomes irregular, respiration is embarrassed, syncope follows with cyanosis, and in severe cases the patients die. This train of events is brought about through the frothing of the blood by the air. The frothed blood in the heart interferes with the action of the valves, and heart-failure is the result.

Primary capillary hæmorrhage.—Capillary hæmorrhage shows itself as a continuous ooze of red blood from many points of a raw surface or mucous membrane. As a rule, it soon ceases spontaneously, and is only dangerous under certain conditions which may be either local or general. The *local* condition causing danger is the large size of the bleeding surface, such as the wall of a large tuberculous abscess after scraping, or the uterus after removal of the placenta; but hæmorrhage from these sources is usually readily arrested by appropriate treatment. Far more important are the *general* conditions, for when these are present capillary hæmorrhage may prove fatal even when the bleeding occurs from a small surface. The most important general causes of continuous capillary hæmorrhage are certain general diseases, such as scurvy, leucocythæmia, certain blood diseases, as Henoch's purpura, and certain chronic intoxications, as jaundice. To these must be added the curious family disease hæmophilia (p. 312). In

all these conditions capillary hæmorrhage may prove fatal in spite of the most careful general and local treatment.

Intermediary hæmorrhage.—This has already been defined as a recurrence of *primary hæmorrhage after it has once ceased, with the* exception of recurrence due to infection. It was formerly defined as hæmorrhage recurring within twenty-four hours of the original wound, but this definition is altogether artificial. The most common cause is the increase of blood-pressure following recovery from the shock of an operation. As shock passes off, the heart beats more forcibly, the blood-pressure rises, and the temporary clot may be displaced from the blood-vessel and the hæmorrhage restarted. Other causes are the slipping of a ligature due to incautious movements on the part of the patient, the increase of blood-pressure due to the giving of stimulants forcing clots out of untied vessels, and bleeding occurring from the distal end of arteries after the establishment of the anastomotic circulation. The symptoms are the same as those of primary hæmorrhage, and the treatment follows along the same lines.

Concealed or internal hæmorrhage.—This form of hæmorrhage is frequently intermediary, occurring after operations on the abdomen or thorax. It also occurs after injury to the various viscera in the abdomen and thorax, and after operations on the rectum or bladder.

The diagnosis mainly rests on the general symptoms and physical signs of hæmorrhage; but the history and local physical signs are often of importance. Thus in the abdomen there may be signs of free fluid in the peritoneal cavity, or dullness on one or the other side; in the thorax there may be signs of fluid in one pleural cavity and compression of the corresponding lung, whilst in the rectum and bladder examination may show these cavities to be filled with blood-clot. *This variety of hæmorrhage is usually extremely dangerous*, and after operation or injury the diagnosis from shock may be very difficult. The treatment is governed by the same principles as apply in the case of external hæmorrhage.

Secondary hæmorrhage.—This form of hæmorrhage is always due to infection, leading to ulceration of the vessel wall or to digestion of the clot. Primary hæmorrhage may or may not be an antecedent.

The condition is perhaps best exemplified by secondary hæmorrhage occurring from the vessels of the stump of an amputation wound which has become infected. As a result of the infection the bacteria or their products bring about a softening of and suppuration in *the thrombi* which had formed in the vessels after the primary operation. This suppuration extends to the walls of the vessels and to the surrounding tissues, and in consequence the thrombosed vessels are opened up,

new vessels are ulcerated into, and hæmorrhage, which may be serious, occurs.

Some hæmorrhages from malignant growths are of the secondary type, when they are due to associated infective processes rather than to the invasion of the tumour growth itself.

The diagnosis of secondary hæmorrhage, which may be either external or concealed, arterial or venous, is made in the same way as the diagnosis of primary hæmorrhage; but there is one point that deserves special mention, namely, the small initial hæmorrhage that frequently precedes the large and often final hæmorrhage. Thus, on dressing an infected amputation stump, the dressing may be found to be stained with blood, although no bleeding is occurring at the time; and this may be repeated two or three times before the vessel completely gives way and fatal hæmorrhage results. These warnings are due to partial opening of the vessel and then re-establishment of the clot, or sometimes to diapedesis of the red blood-cells owing to the severity of the inflammatory processes; they are to be regarded as indicating the need for the immediate adoption of measures to prevent further hæmorrhage; but they are not constant, and a profuse flow of blood terminating fatally may be the first indication of secondary hæmorrhage. In treatment of infective conditions of the limbs by continuous warm baths, secondary hæmorrhage is peculiarly dangerous The limb is placed in a bath which is covered to prevent escape of heat, and it is kept there for hours. Should secondary hæmorrhage occur, the blood may flow into the bath, and as the condition is painless the hæmorrhage may only be suspected when the patient shows marked signs of loss of blood I have met with two fatal cases of secondary hæmorrhage that occurred in this way.

TREATMENT

The treatment of hæmorrhage may be considered under the headings *general* and *local*, the former being concerned with the effects of the loss of blood until it has been replaced, and therefore extending over weeks or months, as well as with its immediate arrest, and the latte with the best means of stopping the loss by local treatment of the bleeding vessel.

General treatment.—The indications for general treatment are as follows:—

1. To produce such conditions as will favour the clotting of the blood in the vessels and so bring about the temporary arrest of hæmorrhage.

2. To keep the brain supplied with blood during the period of actual loss while the patient is in the *condition of shock* due to loss of blood.

3. To supply the actual amount of fluid lost by the hæmorrhage and so maintain the arterial blood-pressure and volume.
4. To stimulate as far as possible the blood-forming organs, so that they may quickly replace both in quantity and quality the blood which has escaped.

The methods of meeting these indications will be discussed under various headings.

Posture.—In the majority of cases of hæmorrhage, especially surgical hæmorrhage, the patient should be placed lying in bed with the foot of the bed raised so that the head is the lowest part of the body, and the pillow should be removed. This posture will favour a good supply of blood to the vital centres in the medulla, without which life cannot continue. The patient should be kept warm with hot-water bottles placed in the bed, but heat sufficient to cause sweating should be avoided. Restlessness, which is often a distressing symptom, should be quietly restrained, and as far as possible the patient should be reassured. In cases of bleeding from a large wound, and when the hæmorrhage can be temporarily arrested, if there is no shock the patient should be anæsthetized as soon as possible to permit thorough aseptic treatment of the wound as well as more secure arrest of the bleeding.

Drugs.—*Morphia*, given preferably by hypodermic injection, is very useful to prevent restlessness and to act as a general sedative, especially in cases where there is severe pain as well as hæmorrhage. It is particularly valuable in those cases of bleeding, such as from the lungs, stomach, or intestine, in which surgical interference is contra-indicated or impossible, and reliance must be entirely placed on the natural temporary arrest, aided by general treatment. It has no direct value in arresting hæmorrhage.

Ergot (or its preparations, or its alkaloid), given hypodermically, causes a contraction of the muscular coats of the arteries, and so diminishes their lumina and the size of the blood-stream; at the same time it raises the blood-pressure by peripheral vaso-constriction and so increases the force of the stream. This general rise of blood-pressure may more than counteract the good local effect of the contracted arteries, and the loss of blood may be increased. This drug is probably only of marked value in bleeding from the uterus. It has the same effect on the unstriped muscular tissue of this organ as on the middle coat of the arteries, and, by causing strong muscular contraction, squeezes the veins and blood-sinuses in the uterine wall and so arrests the bleeding.

Ergot is largely used in midwifery and gynæcology, being particularly valuable in post-partum hæmorrhage, and it has also been used in the treatment of hæmoptysis.

Acetate of lead, tannic acid, gallic acid, adrenalin, and *hamamelis* have all been used as general hæmostatics on account of their vaso-constrictor action; but they are probably of little value, whether given by the mouth or hypodermically.

Fresh blood-serum obtained from horses, dogs, rabbits and human subjects has been given by intravenous and subcutaneous injection in the treatment of hæmorrhage, and is worth a trial in those cases in which the bleeding vessel cannot be controlled, as, for example, in hæmorrhage from the kidney.

Calcium chloride and calcium lactate.—These drugs have been largely used, both in the prophylaxis and in the treatment of hæmorrhage; but their value is doubtful. In the phenomenon of coagulation of the blood calcium salts play a large, though not thoroughly understood, part. Blood deprived of its calcium salts will not clot, and in hæmophilia the blood is said to be deficient in calcium. The rationale of giving calcium chloride or lactate is to supply the calcium lacking in the blood or to increase it in quantity. They have been used in the treatment of bleeding in hæmophilics, and have been largely given both before and after operations to patients in whom difficulty of arresting hæmorrhage was anticipated. Thus they are given to patients suffering from jaundice, pancreatic disease, leucocythæmia, etc. The value of calcium so given in these cases has been much called in question, and many surgeons have discarded its use altogether in jaundiced patients, but others insist on its value and give it in all cases. The questions of its dosage and the length of time during which it is given are probably important, and variations in these may account for some of the discrepancies in accounts of its value. The probability is that it does no harm and can be given in suitable cases without fear. When it is decided to use the lactate or chloride in cases of jaundice, it should be given in 30-grain doses every four hours for a day or two before the operation, and its use continued afterwards for three or four days, either by the mouth or, if this is inadvisable, by rectal injection.

Stimulants.—The effect of stimulants—alcohol, strychnine, caffeine, etc., is to increase for a longer or shorter period the force of the heart's beat. This raises the arterial pressure, if vaso-dilatation does not occur, and will increase the hæmorrhage. Many cases of intermediary hæmorrhage are undoubtedly caused by the injudicious use of stimulants, the increased blood-pressure forcing the temporary clots out of those blood-vessels which have not been securely tied. It may therefore be laid down as a general rule that all stimulants, alcoholic and otherwise, are to be avoided in the treatment of hæmorrhage. The lower the blood-pressure falls, the greater the tendency to the formation of clot in the mouths of the blood-vessels, and in

cases of concealed hæmorrhage and in hæmorrhage from the lungs and intestines the life of the patient depends upon the formation of this clot. To raise the blood-pressure, even for a time, by giving stimulants is bad surgery, and may directly cause the patient's death.

Blood transfusion and infusion.—After all bleeding-points have been secured, the strongest indication in the general treatment of hæmorrhage is to supply the vascular *system with fluid to replace* that which has been lost, and so to re-establish the blood-pressure and the effective circulation on which life depends. By the infusion of a suitable fluid into the patient's vascular system, the blood-volume and blood-pressure are raised towards the normal, the heart is given material to pump upon, and so the circulatory mechanism is encouraged; if the fluid used be a compatible blood, then the number of oxygen-carrying red blood-corpuscles is restored to something like its proper proportion. Transfusion of living blood from another human being into the veins of the patient is therefore clearly indicated; this has been tried at various times for centuries, but only recently has *it been done with anything like uniform success.*

Blood transfusion failed in many cases because clotting occurred in the tubes and containers between the patient and the donor of blood, in others it precipitated thrombosis in the recipient's vessels, whilst in certain cases it set up hæmolysis with resultant rigors, pyrexia, hæmoglobinuria, and death These difficulties have been overcome by improvement of technique, the use of paraffin-coated smooth tubes, reduction of the time occupied in the operation, and especially by the recognition that no animal blood, and only that of certain chosen human beings, is compatible with the recipient's serum. Now, therefore, the method is freely used in cases of severe hæmorrhage, and *also in certain anæmias, such as pernicious anæmia.*

Infusions of blood-substitutes, such as normal saline or gum-acacia saline, restore blood-volume, and therefore have distinct uses in the treatment of pure shock, but they do not replace the oxygen-carrying red blood-corpuscles.

The choice of the donor is important He must be healthy, must have a negative Wassermann reaction, and his corpuscles must not agglutinate in the recipient's serum—i.e. his blood must be "compatible" with that of the patient. Even after injection of a compatible blood, a little reaction is sometimes seen, with a slight or moderate chill and a rise of temperature for a few hours. This is a matter of no danger; but transfusion of an incompatible blood causes dangerous agglutination or hæmolysis, or both. In such cases the patient complains, during the operation, of severe backache, and he suffers from a feeling of distress and of nausea; after the transfusion

he has a rigor and a rapid rise of temperature, may show jaundice and hæmoglobinuria, and may collapse and die.

To prevent this danger, compatibility of the bloods of donor and recipient must be determined beforehand. This may be done in each individual case by mixing red corpuscles of the donor with serum of the recipient and examining for agglutination; agglutination only need be tried, because it has been found that it always precedes hæmolysis, and the test for it is easier than that for hæmolysis. This plan is tedious Moss found that all people can be grouped as regards their hæmolytic and agglutination properties. His findings are set out in the accompanying table:—

Serum Group	*Cells of Group (Donor)*				*No. of individuals in Group*
	I	II.	III.	IV.	
I.	0	0	0	0	5 per cent
II.	+	0	+	0	40 "
III.	+	+	0	0	10 "
IV.	+	+	+	0	45 "

Consideration of this table shows that the corpuscles of a Group I. person are clumped by the serum of any other group but its own; those of Group II. are agglutinated by the serum of Groups III. and IV.; those of Group III. by II. and IV.; but the cells of a person belonging to Group IV are clumped by the serum of no group; such a person therefore is a "universal donor" and can give blood to anyone without danger. A list of such Group IV. people should be kept in every hospital. If only Group IV. donors are used, then the blood of the patient need not be tested. To *determine the grouping,* the investigator should have some known serums belonging to Groups II. and III kept in sterile bottles with the addition of 1 per cent. of chloroform as a preservative. A drop of Group II. serum may be put at one end of a microscope slide, and a drop of Group III. serum at the other; then a little of the blood under test is mixed with each; if the blood belongs to Group IV., no clumping will occur, and the film will remain smooth.

Methods of blood transfusion.—The dangers of hæmolysis and agglutination being avoided by proper choice of a donor, success then depends on a technique which abolishes clotting in the apparatus, etc. Coagulation is accelerated by (1) rough handling and damage to the formed elements of the blood, especially the platelets; (2) by mixture of tissue "juices" with the blood; (3) by passage of the blood over rough surfaces; (4) by the presence of any shreds of fibrin.

and (5) by undue *delay*. *Therefore manipulations* must be gentle, and should not occupy more than fifteen minutes, and the apparatus used should be *smoothly lined with* paraffin and perfectly free from fibrin; or coagulation may be prevented by *drawing the blood into* anticoagulants such as sodium citrate.

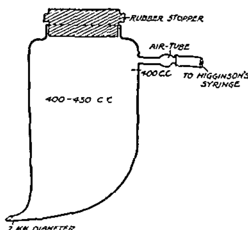


Fig. 32.—Kimpton-Brown tube for indirect transfusion.

One of the following methods may be adopted :—

1. *Use of "whole" blood (unmodified)*.—(1) Direct from artery to vein through silver cannula and a short paraffined rubber tube This plan is not easy; the character of the flowing blood is not seen, and if the recipient be bacterially infected, there is some danger to the donor.

(2) Indirect transfusions may be carried out by means of a number of paraffined syringes, after needles have been put into the veins of both donor and recipient; a syringeful of normal saline should be injected after each charge of blood. This method occupies time, and requres two skilled assistants. Or a syringe with a four-way cock may be used, the ways leading respectively to donor's vein, recipient's vein, a jar of normal saline, and the syringe. This method is quick, but not very simple.


Fig. 33.—V-shaped incision in vein in transfusion.

The plan for indirect transfusion suitable for most cases, and one that can be done with one unskilled assistant, is Marshall's method of using a Kimpton-Brown tube. The characters of this tube are shown in Fig. 32. The tube is thoroughly cleansed with a brush and chloroform, dried with alcohol and ether, and autoclaved; it is then lined with a smooth layer of sterile ether-solution of ordinary hard paraffin of which some is sucked in by means of a Higginson syringe; the warmed tube is rotated and held upside down so that a uniform coat is applied, even to the fitting of the rubber stopper; it is then cooled with cloths soaked with alcohol. The pneumatic cuff of a blood-pressure apparatus is applied above each elbow, and the operator exposes a vein in the donor and another in the

recipient; in each case a ligature is put round the vein above and another below the proposed snip into the vein; these ligatures are not yet tied, but are caused to function by the weight of pairs of forceps hanging to their ends. He then makes a V-shaped snip (Fig. 33) into each vein and lays a gauze pad soaked in saline solution on each wound. Introducing the nozzle of the tube into the donor's vein, and using the Higginson syringe as an extractor, he draws up 400–450 c.c. of blood; then, rapidly transferring the nozzle to the snip in the recipient's vein and reversing the Higginson syringe so that it now

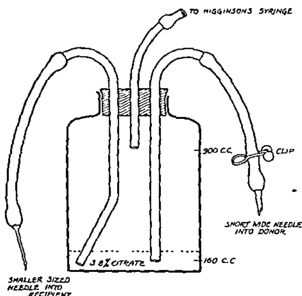


Fig. 34.—Apparatus for transfusion of citrated blood.

acts as a blower, he injects the blood into the recipient, occupying about four minutes in the process. It now only remains to tie the ligatures.

2. *Use of modified (citrated) blood.*—This method has the advantages that one worker alone is needed, and that the time limit of the operation is much lengthened. The apparatus (Fig. 34), with the 160 c.c. of citrate in it, is autoclaved for half an hour at 105° C. at least. The Higginson syringe being used as a sucker, the donor's blood is drawn into the "isocitrate" (= isotonic sodium citrate 3·8 per cent., freshly made with distilled water and filtered). Mixture is obtained by rotating, the apparatus is detached from the donor and is then attached by the other needle to the recipient, then by the use of the Higginson syringe, used as a blower, the citrated blood is injected into the recipient.

3. *Preserved blood-cells* may be stored for long periods in war by

drawing blood into a mixture of previously sterilized 3·8-per-cent. (isotonic) citrate (350 c.c.) and 5·4-per-cent. (isotonic) *dextrose solutions*, and then keeping it in an ice chest.

The Kimpton-Brown tube and the citrate methods are best adapted to civil surgery.

If direct transfusion of blood be not used, other fluids may be given in various ways:—

1. *By the mouth.*—If the patient is conscious and there are no contra-indications, such as bleeding from the stomach or vomiting, fluid (milk, water, albumin-water, etc.) should be given freely by the mouth. The patient should be encouraged to take large quantities of hot liquids, which will be rapidly absorbed from the gastro-intestinal tract and make good the deficiency of fluid in the vascular system. Thirst, which is one of the distressing symptoms after a large hæmorrhage, is relieved in this way, and no limit should be placed on the amount of fluid given to the patient.

2. *By the rectum.*—If the giving of fluid by the mouth is contra-indicated for any reason, warm normal saline solution can be given by the rectum, as it is rapidly absorbed by the mucous membrane. Two or three pints should be run into the rectum by means of a funnel and tube very slowly so as not to act as an enema. It may also be given continuously for hours, about half a pint each hour.

It may be conveniently run in from an inverted thermos flask, through the cork of which are led two tubes, one connected with the rectal tube and the other turned up as an air-tube; Lane's bag, which is an inverted rubber hot-water bottle, also acts satisfactorily.

3. *Subcutaneously.*—Normal saline fluid can also be injected into the subcutaneous tissue, and will be absorbed into the blood- and lymph-streams. In males the loose skin of the groin or axilla is the site chosen, and in females it can be injected under the breast, between it and the pectoral muscles.

4. *Intravenously.*—The injection of normal saline fluid directly into a vein is the most rapid method of supplying fluid to the vascular system, and therefore is to be preferred in cases of severe hæmorrhage. The fluid used is a solution of sodium chloride (common salt) and water in the proportion of 1 drachm of salt to 1 pint of water, *both the salt and the water being sterilized.* Some surgeons add a small quantity of potassium chlorate to the salt and water in order to render it neutral, as acid or alkaline solutions may be dangerous; and some add from 3 to 5 per cent. of dextrose so as to form a nutritive fluid and to favour osmosis from the tissues to the blood-vessels.

Saline fluid that has been injected into the venous system soon passes out of the vessels into the surrounding lymph-spaces and tissues,

and so its value in raising the blood-pressure is lost. To prevent this, Bayliss introduced a solution of gum acacia, but its use is not without danger, and the practical advantage over normal saline solution is doubtful.

Technique of intravenous infusion.—In cases of amputation, or where a large artery is cut across, infusion of saline fluid may be made directly into the vessel, but this has been found to have no advantage over intravenous infusion. The vein usually selected is the median basilic vein of the left arm, as it is generally large and constant in position. The surrounding skin is rendered as sterile as possible in the manner usually employed before an operation. A bandage, or the pneumatic cuff of a blood-pressure apparatus, is wrapped round the upper arm so as to retard the venous return and render the vein prominent. An oblique incision is made across the vein, which is quickly exposed in the subcutaneous tissue, and a double ligature is passed round it and the lower end secured. A small V-shaped snip slit is then made *across* the vein and the cannula introduced and secured in the vein by means of the upper ligature. The bandage or cuff round the upper arm is then removed.

In many cases time may be saved by the introduction of a sharp needle straight into the vein, but even then it is advisable to incise the skin first.

The saline fluid, which should be at a temperature of 105° F., may be injected by means of a syringe with a double way or run into the vein directly from a flask raised slightly above the level of the arm. The infusion should be carried out slowly under slight pressure, and great care taken that no air enters with the fluid, otherwise serious consequences may result. From one to three pints, according to the amount of blood lost, the age of the patient, and the degree of shock, should be infused

If during the infusion the patient should become dyspnœic and cyanosed, or suffer from syncope, the infusion must be at once stopped, and artificial respiration carried out if necessary.

When sufficient fluid has been injected, as shown by the state of the pulse, the cannula is removed and the proximal end of the vein tied. The wound in the arm is sutured and a light dressing applied. It should be remembered that the brachial artery lies immediately beneath the vein, separated from it by the bicipital fascia, and that injury to this artery may result in an arterio-venous aneurysm. Intravenous saline infusion is sometimes followed by a mild rigor and a slight rise of temperature, but there are no permanent ill effects.

It must be clearly understood that the infusion of fluid is contra-indicated until the hæmorrhage has finally ceased and the vessel

has been securely closed, although Crile believes that direct transfusion of blood will bring about an arrest of hæmorrhage, as well as relieve its consequences.

After a severe hæmorrhage that does not terminate fatally, the *blood-serum* is rapidly restored by absorption of water, albumin, and salts from the tissues; but the restoration of the red blood-corpuscles takes longer. These corpuscles are manufactured by the red bone-marrow of the long bones and the vertebræ. In young subjects regeneration begins after forty-eight hours, and the process, even following a severe hæmorrhage, is complete in six weeks, and often sooner; but, as has already been pointed out, in the elderly and aged a serious loss of blood seldom ends in complete recovery, the patient remaining permanently anæmic.

After a loss of blood the patient should be placed under the best hygienic conditions, with plenty of fresh air and sunlight. The diet should be plentiful, light, and nutritious; whilst iron, arsenic, and cod-liver oil should be given.

No drugs are known to act specifically upon the blood-forming organs.

First-aid treatment of primary arterial hæmorrhage.—The wound should be thoroughly exposed and the thumb *of one hand pressed firmly into it, pressure being made,* if possible, directly on the spurting artery. This is frequently sufficient to stop the hæmorrhage; *but if not, or if the vessel cannot be compressed* in the wound, the thumb of the other hand should make firm pressure on the main artery supplying the area in which the wound is, *nearer* the heart than the wound, the artery being firmly compressed against an adjacent bone Each of the main arteries has its special place where compression can be most readily and effectually carried out, and the most severe hæmorrhage can usually be arrested *temporarily* in this way, exceptions being the very large arteries, such as the aorta or the innominate.

Digital compression, as described above, will be found to be very tiring, and cannot be maintained for very long, so as *quickly as possible* a tourniquet should be improvised and firmly secured round the limb above the bleeding-point, care being taken that it is *sufficiently* tight to arrest the arterial flow, and not merely to compress the veins and so increase the amount of blood lost A tourniquet can *only* be left in position for about two hours, as a longer application than this causes danger of gangrene, and the pressure is usually very *painful*. Therefore it should be removed as soon as possible, the vessels being tied to prevent hæmorrhage. Although the first indication *in hæmorrhage* is to arrest the bleeding, yet the rules of asepsis should not be neglected.

Deliberate treatment of primary arterial hæmorrhage.—Three rules may be laid down as the principles on which primary arterial hæmorrhage is treated:—

1. If the hæmorrhage has stopped spontaneously, **no further treatment is necessary.** Of course, it must be understood that during the necessary routine cleansing of an accidental wound the hæmorrhage may be restarted, and then the treatment laid down by the next two rules must be carried out.

2. **Secure the bleeding artery in the wound.**—The bleeding vessels should be secured with hæmostatic forceps and ligatures applied, the wound being enlarged, if necessary, to facilitate this operation. Ligature of the artery in continuity, though sometimes easier than ligature of the bleeding-point, should not be done for several reasons: (1) The necessity of making a second wound should be avoided, especially as the operation is one of urgency, and it may be impossible to take full aseptic precautions; (2) ligature of the main artery of a limb may be necessary and may lead to gangrene; (3) ligature of the main artery may not stop the hæmorrhage if an extensive anastomotic circulation is present; (4) the source of the artery that is bleeding may be difficult to determine and the wrong artery may be ligatured in continuity. A patient died from hæmorrhage after ligature of the superficial femoral artery in Hunter's canal to stop bleeding from a deep punctured wound on the inner side of the thigh At the autopsy the severed artery was found to be a branch of the profunda femoris

In certain situations, especially in the case of deep punctured wounds, ligature of the main artery in continuity is the correct treatment, as exposing the severed vessel and ligaturing it *in situ* might cause serious damage to surrounding structures These situations are—

(1) *The palm of the hand*, when the bleeding comes from the deep palmar arch. Here ligature of the radial *and* ulnar just above the wrist or the brachial in the arm is to be preferred to local ligature, which would involve a dissection damaging to the numerous tendons and tendon sheaths in the palm of the hand.

(2) *The face and neck*, in bleeding from the deep branches of the external carotid, such as the internal maxillary or the occipital as it lies deep to the mastoid process Many of the subdivisions of the branches of the external carotid run in bony canals, and their ligature would be exceedingly difficult and would necessitate serious damage and disfigurement; hence ligature of the main artery at the seat of election between the superior thyroid and the lingual branches is to be preferred.

(3) *The branches of the internal carotid.*—These arteries are found inside the cranium, supplying the brain, and ligature *in situ* is impos-

sible. If a diagnosis is made and treatment is attempted, either the common or the internal carotid artery should be ligatured in the neck.

The stoppage of hæmorrhage by means of ligatures, torsion, pressure, suture, etc., is discussed at p. 278.

3. **Secure both ends of the severed artery.**—This should be done even when *hæmorrhage is not occurring from the distal end* of the artery at the time the wound is treated. It not infrequently happens that hæmorrhage occurs from the distal end of an artery when the anastomotic circulation is established or when shock has passed off; indeed, this is the most frequent cause of intermediary hæmorrhage.

First-aid treatment in primary venous hæmorrhage.—The wound should be freely exposed and pressure made with the thumb directly on the bleeding-point. In the case of bleeding from a limb, the part should be elevated and care should be taken that there be no constriction between the wound and the trunk. A pad should be placed on the wound and a bandage carried up over the pad from the extremity of the limb. No tourniquet should be used in the first-aid treatment of venous hæmorrhage.

Deliberate treatment of venous hæmorrhage.—This consists of picking up the vessel in the wound with hæmostatic forceps and applying a ligature as for arterial hæmorrhage; but carefully graduated pressure can usually be relied upon to arrest venous hæmorrhage, *which is only serious when it comes from the largest venous* trunks or from varicose veins. Bleeding from a cerebral sinus can be arrested by carefully packing the sinus with gauze.

Treatment of air in veins.—During an operation involving danger to the great veins at the root of the neck, which are influenced by the respiration, the wound should be *kept flooded with saline solution*, so that, in the case of injury, fluid and not air may be sucked in. Air in veins is not necessarily dangerous, the danger depending upon (1) the amount of air entering, (2) the speed with which it enters, (3) the distance from the heart at which it enters.

Directly the characteristic noise of air entering a vein is heard, the wound in the vessel should be closed and a ligature applied as quickly as possible. If the right heart becomes seriously embarrassed, artificial respiration should be at once begun, as the condition frequently ends in death.

Senn advised *puncture and aspiration of the right ventricle*, or, if the air has entered by the jugular vein, catheterization and aspiration of the right auricle—both somewhat drastic measures. Stimulation of the vagus has been recommended, but most surgeons depend mainly upon artificial respiration.

Treatment of capillary *hæmorrhage.*—Capillary hæmorrhage is rarely dangerous in the normal individual, and can usually

be arrested by pressure or the use of hæmostatics. The most important of these are cold (ice-cold water), hot water at 120° F., adrenalin chloride, tannic and gallic acids, and calcium chloride. None of these should be applied in such strength or for long enough seriously to damage the tissues. In some cases the application of the cautery at a dull-red heat so as to char the tissues is the best method of arresting capillary hæmorrhage.

Treatment of intermediary hæmorrhage.—The methods of arresting intermediary hæmorrhage are precisely similar to those for arresting primary hæmorrhage, which it exactly resembles; but *concealed* hæmorrhage, which is frequently intermediary, demands a special word. In cases of abdominal hæmorrhage, especially occurring after operation, a second operation for the arrest of hæmorrhage cannot always be undertaken at a moment's notice, and yet the bleeding may be severe. The patient should be placed with the head lower than the trunk and limbs, and then the limbs carefully and firmly bandaged from the extremities to the trunk, so as to drive the blood to the vaso-motor centres in the brain.

Blood transfusion in these cases may be necessary after the bleeding-point has been secured.

Treatment of secondary hæmorrhage.—The treatment of secondary hæmorrhage differs in one important point from the treatment of primary hæmorrhage: no matter how slight the hæmorrhage may be, or whether the hæmorrhage has stopped when the patient is seen, the treatment must be to secure firmly the artery, as a small preliminary hæmorrhage may be the precursor of a large and fatal one

The most satisfactory method of treatment, and the method to be adopted whenever practicable, is to open up the wound thoroughly after applying a tourniquet, and place a ligature on the bleeding-point, opportunity being taken to render the wound as aseptic as possible, and so to bring about healing without danger of further hæmorrhage. This method is not always possible, for the following reasons:—

1. The tissues may be so sloughing that the ligature will not hold. The actual cautery, at a dull-red heat, may be applied, or in some cases it may be advisable to re-amputate higher up the limb.

2 The hæmorrhage may be an oozing from numerous small vessels, which it will be impossible to ligature. In this case the application of the actual cautery, or packing the wound with sterile gauze, will usually arrest the bleeding.

3. In cases of secondary hæmorrhage from large vessels in the groin, abdomen, and neck it may not be possible to expose and ligature the bleeding vessels. The wound should be carefully packed with aseptic gauze, which should be left in position for several days.

4. Hæmorrhage from malignant growths which have fungated is difficult to control by ligature, as even if the vessel is seen the ligature will not hold in the breaking-down tissue. Ligature of the main artery in continuity is the best treatment, but the advisability of doing this and prolonging a patient's life for a few weeks is doubtful. In the case of secondary hæmorrhage occurring from an artery ligatured in continuity the wound should be opened up and a ligature placed on the artery above and below the bleeding place.

HÆMOPHILIA

Under this term many different conditions have been described, all of which have the common factor that the subject has a tendency to bleed readily and profusely, either spontaneously or from slight injuries. They have been recorded in both men and women and at all ages, and much confusion has arisen from including them all under the term "hæmophilia." This word has been so loosely used that it has come almost to mean profuse hæmorrhage from a trivial or unknown cause; but it is important to limit it to one class of case only, and to endeavour to find an exact pathology for bleeding occurring from some other cause.

Definition.—"Hæmophilia" should be limited to the family bleeding disease which only affects the males of a family and has a definite characteristic method of inheritance The main features of this disease will be first described, and then some reference made to other cases of profuse bleeding which do not come into this category. The condition is a congenital tendency to almost *uncontrollable* bleeding, nearly always from some slight injury, but perhaps occasionally spontaneous; *the hæmorrhage may take place from the external* surface of the body, from the mucous membranes, into serous or *synovial cavities, or into the tissues generally, with formation of* ecchymoses.

The *hereditary or family characters of this* disease are well marked. The sporadic cases published from time to time do not *belong to this disease*, and the inheritance is almost constant in its peculiarities.

The daughters of a bleeder-father do not suffer from the disease, true hereditary bleeders never being females, but they transmit it to their sons; and if there are several daughters in a family, all or some, or even only one, may transmit it; or the disease may intermit a generation entirely. The daughters of "bleeders" generally have large families. The sons of a bleeder-father do not usually suffer from the disease, nor do they transmit it either to their sons or daughters; but cases have been published which make it impossible to say that the disease *is* never transmitted directly from father to son. These cases, however,

are doubtful, and belong to the past; *they probably represent errors* of observation, or are based on very insufficient grounds.

As has been stated above, females do not suffer from the true family disease, although some authors have stated that they do, one giving the ratio of males to females as 197 to 15 or 13 to 1.

Nearly all the families affected with this disease that have been traced belong to the Anglo-Saxon race, but instances in the Latin race are known, although few cases are reported in French literature. The inheritance in one South African family has been traced through eight generations.

The cause of the disease is quite unknown, and there is no constant pathological anatomy, although several conditions have been described. In some cases it is stated that the aorta and the large arteries are abnormally small, so that the blood-pressure is high and difficulty of arrest of hæmorrhage follows. Abnormal thinness and degeneration of the arterial walls have been stated to be the cause of the spontaneous hæmorrhage, while some authors describe a defective muscular coat of the arteries, so that contraction of their walls is slight or absent. Others, again, have looked to the composition of the blood to discover the cause of [illegible] coagulation period or have [illegible] to the absence of calcium salts [illegible], in any way explains the disease, and they are not constant in every case. In many cases the coagulation of blood is normal in time and the coagulum firm.

Symptoms.—The symptoms of the disease are persistent hæmorrhages following slight cuts or bruises or occurring spontaneously, and dating from birth. The bleeding continues until death occurs, or more usually until spontaneously arrested. Hæmorrhage from the umbilical cord may occur, although it is rare, and starts shortly after severance of the cord; it may be fatal. Vaccination is not followed by hæmorrhage, but the eruption of the milk and permanent teeth is always attended with danger; removal of a tooth may lead to uncontrollable hæmorrhage. Cases in which the disease first appears in adult or in late life are probably not cases of the true family disease. The injuries that cause the bleeding are often of the most trivial type, such as the removal of a tooth, a leech-bite, a prick from a needle, or a cut while shaving. The bleeding may be arrested for a time; but it may recur again and again until the patient dies, though recovery is the rule. It is a curious fact that the tendency to hæmorrhage is not constant, and a well-marked bleeder may injure himself and not bleed more than a normal person, although at other times very slight pressure on the skin will determine a large ecchymosis.

Bleeders are said to have extraordinary recuperative powers, and

also great capacity for withstanding the loss of blood, and as the patient gets older the tendency to bleed is diminished and in some cases may disappear.

The skin lesions vary from a bruise to a large hæmatoma; there is no purpuric rash similar to that seen in cases of purpura hæmorrhagica, which is sometimes mistaken for hæmophilia.

The hæmorrhage which occurs into *joints* deserves special mention, as the disease used to be described as associated with a chronic arthritis. This arthritis is solely due to hæmorrhage into the synovial cavity of the joint, the knee- and elbow-joints being those usually affected. The physical signs in a recent case are those of a subacute arthritis with effusion, which gradually subsides; but after repeated hæmorrhages the joint, both clinically and pathologically, resembles that of a case of chronic osteo-arthritis, or even a chronic tubercular arthritis.

Operations on these joints under a mistaken diagnosis, or in order to strengthen the limb and get more movement, have been followed by fatal hæmorrhage.

Treatment.—Children who inherit the disease, or even come of a bleeder family, should be carefully guarded against all the common accidents of childhood, for prophylaxis is of the utmost importance. Every form of surgical operation is contra-indicated, except those which are absolutely necessary to save life The daughters of bleeders should not marry.

The treatment of the hæmorrhage when it occurs does not differ in principle from the treatment of hæmorrhage occurring in the non-hæmophilic, but every method should be tried in succession, except that no operation, such as ligature in continuity, should be done, and more trust should be put in hæmostatics and general treatment by drugs.

Calcium chloride and calcium lactate have been advised by Wright to increase the coagulability of the blood, but the value of these drugs is doubtful. Others have tried the injection of human serum, dogs', horses', and rabbits' serums, or antidiphtheritic serum, but these appear useless in the true family disease, although they may be of service in profuse hæmorrhage from other causes.

Finch advises venesection, and irrigation of the wound with hot water; and Crile recommends direct transfusion of human blood, both to stop the hæmorrhage and remedy the loss of blood. Transfusion of blood from the patient's mother is worth trial, not only for the replacement of blood, but because, being capable of transmitting hæmophilia without herself suffering from it, she may possibly possess some antihæmophilic property in her blood.

The most-used *hæmostatics* are adrenalin (both internally and

externally), ethyl chloride, ferric chloride, hydrogen peroxide, hot water, powdered chalk, and calcium chloride. All should be tried in turn, and all may be found equally useless.

No drug, used either externally or internally, is a specific, and some patients die of loss of blood in spite of all treatment.

In the case of a large wound in a hæmophiliac, Thiersch recommends the avoidance of sutures and compressive dressing, and allows the wound to fill with blood-clot, which is left undisturbed.

Conditions simulating hæmophilia.—Surgical literature teems with cases of patients who have bled profusely after injury or spontaneously; and these cases are often described under the title of "hæmophilia," although there is no trace of a family history of bleeding, and often the hæmorrhage only occurs once in the patient's life. The more carefully the cases are investigated the more it is seen that they differ essentially from family hæmophilia. In women (who never suffer from hæmophilia) the bleeding is usually from the uterus, is associated with menstruation, and is in many cases due to abortions, fibroids, carcinoma, etc. Other cases of hæmorrhage under the skin and sweating of blood occur in neurotic women, and are well-recognized stigmata of hysteria. Hæmorrhage from the umbilicus in the newly born is often associated with infection, while severe hæmorrhage after removal of a tooth may be due to injury of the dental arteries, which is difficult to control on account of their passage within bony canals.

Scurvy, scurvy rickets, Henoch's purpura, purpura hæmorrhagica, jaundice, pancreatic disease, etc., also account for many so-called sporadic cases of hæmophilia, which should not be diagnosed unless the family history is known.

SHOCK

Shock is a condition of general depression of vital functions, associated with low blood-pressure. Since the introduction of anæsthetics and the aseptic and antiseptic methods of operating, surgical shock is the chief danger that the surgeon has to combat; but in spite of all the experimental and clinical investigation devoted to this subject during the last few years, it is impossible to give a completely satisfactory definition of the condition, and there are still obscurities in its essential pathology. Recent advances, however, have enabled a distinction to be made between two kinds of shock, entitled Primary and Secondary.

Primary shock appears immediately after injury, is analogous to fainting, is probably of nervous origin, and is perhaps associated with cardiac inhibition by the vagus. *Secondary* shock occurs an hour or two after injury, and is associated with wounds involving consider-

tissue damage. In it nervous factors are less prominent, and ably the condition is essentially a stasis in capillaries due to rption from the wound area of toxins which, according to Dale, analogous to histamine.

ETIOLOGY

s already mentioned, primary shock is probably nervous in n *and associated with vagal cardiac inhibition*; while secondary is a condition of depletion of blood volume by toxic stasis in laries. It is met with in many and varied conditions, but it happens that two or more causes are present at the same time, it may be difficult to determine which of them is the most rtant factor. For example, in a severe accident crushing a limb, stimulation of peripheral nerves and a large loss of blood are associated as the agents in the production of a severe degree ock. Predisposing causes of shock may be—

A disturbance of the higher nerve-centres, either ed by a sudden mental "shock," such as the hearing of bad or by the anticipation of some severe injury, e g. the fear of eration. This mental disturbance is sufficient in itself to produce found condition of shock, even ending in death, and there are cases on record of patients dying after the simplest of opera- owing to intense fear On the other hand, severe and even lesions may be sustained without the immediate supervention ck, if the patient's mind is so intensely concentrated on some- else that the lesion passes almost unnoticed. This temporary nity may be followed by "delayed" shock when the condition ense concentration has ceased.

Extensive cutaneous lesions, e g. burns and scalds. mount of shock following a burn largely depends on the extent burnt surface, and not so much on the depth of the burn. This bably due to the intense stimulation of the cutaneous nerves of in, followed by over-stimulation of the central nervous system. following exposure to cold is due to the same condition At the time, other factors probably help to produce a fatal result in cases, such as poisoning by carbon monoxide and other toxins ed from the burnt area, loss of the excretory power of the nd congestion of the internal organs.

Injuries to large nerve-trunks.—Injuries involving ng of the large nerve-trunks are usually associated with a severe of shock. This depends in part on the severe pain of these s, pain being very potent in inducing and maintaining shock, rtly on the destruction and over-stimulation of a large number rent nerve-fibres. If the path of impulse up the nerve-trunks

has been previously blocked by injection of cocaine, the shock is not so severe.

4. **Extensive crushing injuries to muscles.**—It was found in the late war that shell wounds which caused extensive laceration of muscle without injury to bone or any vital structure or organ were frequently fatal within a few hours.

5. **Hæmorrhage.**—Loss of blood is connected in several ways with the condition of shock. In severe injuries both shock and hæmorrhage are frequently present, and it is often difficult to estimate the degree in which each contributes to the patient's condition. Both are associated with a fall in blood-pressure, and while shock may be directly dependent upon loss of blood, on the other hand loss of even a small amount of blood while the patient is in a condition of shock is apt to be fatal. As the treatment of hæmorrhage differs from that of shock in material points, a differential diagnosis is of the utmost importance.

6. **Sudden severe irritation of extensive serous membranes,** e.g. the peritoneum. The rupture of a gastric, duodenal, or typhoid ulcer, or the bursting of a hydatid cyst or an abscess into the general peritoneal cavity, is usually followed by so profound a condition of shock as to obscure the diagnosis of the lesion. This shock is probably produced in the same way as the shock following an extensive cutaneous lesion, i.e by over-stimulation of a large number of sensory nerve terminations

7. **Severe blows on the abdomen and thorax,** not connected with any serious internal lesion. A severe blow on the abdomen may cause death from shock, and on post-mortem examination no gross lesion may be found. The shock probably depends on over-stimulation of the peripheral sympathetic plexuses, such as the solar plexus.

8. **Manipulation,** especially intermittent tension on the blood-vessels and nerves of exposed viscera. The production of shock by this method is frequently met with during the necessary manipulations in operations on the abdominal viscera, particularly when the parietal peritoneum and the mesentery are interfered with, and it constitutes one of the great dangers of abdominal operations. Under this heading must also be placed the shock associated with intussusception, strangulated hernia, etc. It is a method frequently used to produce shock during experimental investigation of the condition.

9. **Exposure to cold** is sometimes a very important adjuvant cause. The shocked patient's temperature is subnormal because his metabolism and therefore his heat-generation are reduced, and also because he suffers rapid reduction of surface temperature. If, in addition, exposure to cold is permitted, shock is increased. Therefore adequate warming is an important part of treatment.

10, 11. **Lack of water** and **mental and physical exhaustion** strongly predispose to shock, as was frequently found in the late war.

12. **Head injuries.**—The condition of concussion following an injury to the head is the condition of shock, and no distinction is possible between them. The clinical symptoms of the two conditions are precisely similar, and depend on the same disturbance of the cardiovascular system.

13. **Injuries to the spinal cord.**—In fracture-dislocations of the spine, with crushing of the spinal cord, shock is usually a marked feature, and may cause death in a few hours.

14. In many **acute infective conditions** shock is often present, as, for example, in the onset of acute infective pancreatitis, and many of the symptoms of acute toxæmia are those of shock; but it is advisable that a distinction be made. In infective pancreatitis, and in other infective conditions within the abdomen, besides the toxic absorption that occurs there is also the intense irritation of the sympathetic nerve processes by the inflammatory lesion, and it is the over-stimulation of these nerves that produces the shock, and not necessarily the absorption of toxins. In acute spreading inflammatory conditions, such as malignant œdema, shock is not manifest, although in the later stages of the disease there is cardiac failure and many of the clinical phenomena of shock are present. The heart-failure in these cases depends at least as much on the weakness of the heart muscle as on disturbance of the central nervous system. Shock is essentially a temporary condition, a step towards death, which is capable of being arrested and may pass off so completely in a few hours that the patient shows no signs that he has ever been through it, although equally in a few hours it may end in death. Infection, on the other hand, causes changes throughout the whole of the body, and recovery will take weeks or months.

PATHOLOGICAL ANATOMY

The pathological anatomy of shock has been the subject of much controversy, especially as to the condition of the cerebral circulation. Some writers have found constriction of the blood-vessels and an anæmic brain, others dilatation of the vessels and a congested brain, and the difference in the post-mortem appearances seems to depend on whether the skull or the abdomen and thorax be opened first. The conditions observed in the human subject during life and in experiments on animals all tend to show that in shock there is a lowering of blood-pressure, to 80 mm. Hg or lower (in man); the extent to which the blood-pressure falls below normal range may be taken as an indication of the degree of shock present. The fall in arterial

pressure is progressive as shock deepens, and rises coincidently with recovery.

In pure shock, without hæmorrhage, the number of blood cells per c mm. is increased; this cellular concentration is much greater in capillaries than in veins—a point in favour of the view that in shock the capillary stasis predominates over the venous stasis; moreover, the engorgement of the veins of the splanchnic area, formerly regarded as the principal factor in surgical shock, is not actually observed by abdominal surgeons.

While the capillaries are dilated and engorged with blood, exudation of serum occurs through their walls, leading to a concentration of the red blood-corpuscles, and this exudation is increased if saline fluid is injected into the venous system.

The condition of the arteries has been the subject of much controversy. Crile and his followers believe that there is marked vaso-dilatation due to inhibition or paralysis of the cardio-vascular centre, whilst Malcolm and other observers state that there is vaso-constriction, the constriction of the arteries being an attempt to compensate for the loss of "effective blood" in the circulation.

Estimation of the total blood-volume shows diminution, sometimes to 50 per cent. of the normal. The fluid elements are reduced, and the blood is concentrated.

SYMPTOMATOLOGY

Mental.—The patient in shock is in a condition of mental torpor, but, unless under the influence of an anæsthetic, is perfectly conscious and able to talk and answer questions rationally. As a rule, there is great anxiety and a fear of impending death; but the expression of the fear is dulled by the mental torpor, and usually the only physical expression of the fear is a wrinkling of the forehead. In some cases, however, there is restlessness, and the patient may be in a state of great excitement, and even act maniacally.

Musculature.—With the exception of the last-mentioned cases the musculature is relaxed, the patient lying perfectly quiet and not moving unless disturbed.

Pulse.—The pulse is usually rapid, but it may be slow, the most characteristic features being weakness, low tension, and small volume. The heart-beat is feeble, often irregular, and not all the beats may reach the radial pulse.

Respiration.—The respiration is shallow, slow, and often irregular. Careful observation may be necessary to be sure that the patient is breathing

Pallor.—The patient is pale and slightly cyanosed, so that he presents a leaden-grey colour, and his body and face are bathed in a cold, clammy sweat.

Temperature.—The temperature, taken in the axilla, is usually subnormal, but if the rectal temperature be taken it is often found to be raised. The fall of temperature is on the whole more marked in secondary than in primary shock.

Sweating.—Sweating is often very profuse, and adds to the loss of fluid from the body.

Pupils.—The pupils are usually slightly dilated, but react to light. If the shock is associated with head injury the pupils may be different in size, or they may be contracted. The *conjunctival* reflex is present.

Thirst.—This is a salient feature, and is probably due to loss of blood from the effective circulation. Thirst is especially recorded in *secondary shock.*

Sphincters.—The sphincters are usually relaxed, the patient passing his urine and fæces under him; but not infrequently retention of urine is present. The amount of urine is diminished in quantity, the kidneys sharing in a general functional depression of all the organs of the body.

PATHOLOGY

An examination of the symptoms of shock, its pathological anatomy, experiments performed on man and animals, and clinical investigations, all go to show that the most important phenomenon is a fall in the blood-pressure associated with banking up of the blood on the capillary and venous side, with corresponding emptiness of the arteries, and accompanied by weakness of the heart's action. That the fall of blood-pressure and weakness of the heart's action is *not* due to cardiac muscle-exhaustion is shown by the fact that if the heart muscle is appropriately stimulated it will still contract quite as forcibly as if the animal were not in a condition of shock. In the same way, it can be proved that the phenomenon is not due to exhaustion of the peripheral ganglia of the heart, as stimulation of the nerves to the heart will still result in a normal response, and the heart can be made to beat forcibly with a corresponding rise in the blood-pressure. Cardiac inhibition has also been assigned as a cause, but severance of the inhibitory nerves does not lessen the amount of shock; and it is now generally believed that shock depends on a disturbance of the cardio-vascular centres in the medulla.

The amount of shock present is best estimated in terms of the peripheral blood-pressure, a fall in which may be produced in two ways by changes in the cardio-vascular centres—namely, by an inhibition, or by a temporary fatigue-paralysis, of the vaso-motor centre.

This view of a paralysis of the vaso-motor centre due to fatigue

or inhibition is not accepted by all writers. It has been pointed out that the cold skin of patients in shock shows a peripheral vaso-constriction which could not occur if the vaso-motor centre were paralysed. This objection can be met by assuming that the coldness of the skin is due to empty arteries and capillary and venous stasis, and the cyanosed appearance of the patient supports this view If the view of central depression be accepted—and certainly it conveniently explains the phenomena of shock—an examination of the causes of the condition given above shows that the inhibition or paralysis may be brought about in the following ways:—

1. By a direct effect from the higher nerve-centres in the cortex on the lower centres in the medulla.
2. By over-stimulation of a large number of sensory nerves.
3. By loss of blood.
4. Reflexly by over-stimulation of the peripheral nerve ganglia, especially those of the abdomen.
5. By direct injury to the central nervous system.
6. By toxic absorption.

It is in this way, it is believed, that *secondary shock* is caused With extensive damage to the tissues, and especially extensive laceration of muscles, toxic substances which have little or nothing to do with microbic infection are absorbed into the blood, and the absorption of these toxic substances plays an important part in the production of shock. From observation and experiment the toxic substance is believed to be histamine (Dale), as already stated. If this view is accepted, it will have an important bearing on the treatment of extensively lacerated wounds of muscles.

TREATMENT

It cannot be too clearly and emphatically laid down that the condition of shock is temporary, whether it be due to inhibition of the nerve-centres or to fatigue-paralysis of them, and that recovery is dependent upon the patient living long enough for the centres to recuperate or the inhibition to pass off. The condition is not only capable of spontaneous recovery, but the patient usually does so recover, and in twenty-four hours or less may show no sign that he has ever been in the condition of shock.

The treatment of shock therefore consists (1) in preventing the condition; (2) in maintaining a blood-pressure sufficient to allow the continuance of the heart's action during the time that the vaso-motor centres are recovering (and that without stimulation of these centres), and to aid their recovery by affording them a sufficient supply of blood.

1. Prophylactic treatment of a patient about to undergo a severe operation. Mental.—Owing to the effect of the higher centres on the lower, it is of great importance to control the feeling of fear present in most patients before an operation, for a trivial operation performed on an intensely frightened patient may be fatal from shock. The patient should be reassured in every way and the gravity of the operation minimized as much as possible. Prolonged waiting before an operation is *inadvisable*.

Warmth.—Exposure to external cold, itself a cause of shock, and the fall of body temperature that accompanies shock, should as far as possible be prevented by external warmth. The patient should be as warmly clad as is consistent with the operation to be performed, and the operating room should be suitably heated (75° F.). For children and elderly people a hot-water bed is advisable, and, if the operation is on the abdomen, the chest and limbs should be wrapped in cotton-wool.

Food.—The time of the preliminary starvation before the administration of an anæsthetic should be shortened if much shock is expected, and in children and elderly people it should not exceed four hours. Nutrient enemata may also be given before an operation, but their value is slight. The aperient given should be a mild one

Anæsthetics.—*It has been seen that one of the chief causes of* shock is an overwhelming number of sensory impulses reaching the brain, and this cause is important, even if the patient is totally unconscious under general anæsthesia. These impulses can, however, be prevented from reaching the brain by blocking the nerve paths up which they travel. This block can be brought about by injecting local anæsthetics (cocaine, eucaine, novocain) into the main nerve-trunks supplying the part to be operated upon, or by operating under local anæsthesia. The use of spinal anæsthesia in preventing shock is under discussion There can be no doubt that the manipulation of the abdominal viscera is very easy under spinal anæsthesia, and this easy manipulation diminishes the time of the operation and the handling of the intestines, but at the same time it must be recognized that a very serious fall in blood-pressure often occurs shortly after spinal injection. This method of securing anæsthesia is most useful in operations on the lower abdomen, pelvis, and lower extremities.

Opinions also differ as to the relative values of ether and chloroform. For the immediate result ether is better, its stimulating effects improving the pulse tension, but the reaction that follows is severe. Chloroform, on the other hand, depresses the heart and reduces the blood-pressure, but there is no reaction to be feared. Other factors, such as the condition of the lungs, must be considered in deciding on the anæsthetic to be used. The most satisfactory anæsthesia to

employ in cases of shock is a nitrous-oxide gas and oxygen mixture. The avoidance of cyanosis is important.

Stimulants.—The question of the treatment of shock by the administration of stimulants will be discussed later; but here it may be stated that the use of stimulants before an operation is probably of little good, and possibly may be actually harmful.

Saline fluid.—In those cases where, before the operation, a large quantity of fluid has been lost from the body, either by hæmorrhage, vomiting, or diarrhœa, it may be replaced by transfusion of blood or the injection of saline fluid; but this point will be discussed under the treatment of shock when it has supervened.

2. **Treatment of shock.**—As the condition of shock is associated with exhaustion or inhibition of the cardio-vascular centres in the brain and is measured by the fall in the blood-pressure, the rational treatment of the condition is to give time for the centres to recover, to supply them with blood, and to maintain the blood-pressure during the period of recovery without calling upon the nerve-centres for further work. For these purposes the following means are employed:—

(1) **Rest.**—If sufficient time of rest can be secured the condition of shock will always pass off, as shock is a temporary condition and recovery is complete. The patient should be kept in bed lying down and absolutely at rest, everything—even changing his position—being done for him. As there is usually muscular relaxation, rest is, as a rule, easy to secure; but in shock with restlessness the problem is more difficult and it may be necessary to give narcotics.

(2) **Narcotics.**—These are given in the cases of shock with restlessness, to procure rest and sleep and so prevent exhaustion; but they are also used for the relief of pain. Pain is one of the great causes of the maintenance of shock by its depressing effect on the brain and by preventing sleep and rest. The administration of morphia or some other narcotic which will diminish restlessness and relieve pain is very valuable in the treatment of shock, especially if it be due to severe crushing accidents, or to burns or scalds.

(3) **Warmth** is as valuable in the treatment of shock as in its prevention. The patient should be wrapped in warm blankets and surrounded by hot-water bottles in the bed, so that the body temperature is maintained by external means. At the same time, it is easy to overdo the application of heat, for too great warmth will dilate the arterioles, producing severe sweating and a further drop in the blood-pressure. Hot-water bottles should not be placed too near the patient, especially if he is under the influence of an anæsthetic or narcotic, otherwise burning may result.

(4) **Posture.**—The patient's bed should be raised at the foot, so that the head is the lowest part of the body. This position will render

it easy for the blood to reach the brain, and will tend to keep the exhausted nerve-centres supplied with blood.

(5) **Stimulants.**—When it was considered that shock was largely due to weakness of the heart's action, stimulants, such as alcohol, strychnia, and caffeine, were very largely used in its treatment; but, although some surgeons still use them, experimental and clinical research has of recent years thrown great doubt on their value in all conditions of shock and has even led to a widely-held opinion that in the severer forms they are harmful. *Strychnia*, which has been *most largely used, mainly raises the blood-pressure by stimulating the* centres in the medulla, and these in a condition of shock are inhibited or exhausted by over-stimulation. Strychnia in the lesser degrees of shock will undoubtedly *raise the blood-pressure for a time*, so that the pulse improves, the heart beats more forcibly, and the peripheral vessels become constricted; but the effect is temporary and is followed by a greater depression than before owing to the further exhaustion of the centres by the stimulation. Repeated injection is followed by less and less effect till none at all is produced, and the centres are still further depressed with increase in the condition of shock. Strychnia will certainly be more useful in collapse with inhibition than in shock with exhaustion; but its value is problematical in both conditions and its harm certain. The hypodermic injection of strychnia in severe cases of shock is not without danger of strychnia-poisoning, as the drug may accumulate owing to the depressed circulation, and as the condition of shock passes off may be swept into the circulation and produce its toxic effect.

The administration of *alcohol* will produce a temporary rise of blood-pressure by its stimulating action both on the heart and on the *central nervous system, but it also causes peripheral* vaso-dilatation with a corresponding fall in the blood-pressure. The stimulating effects are quite transient, and leave behind an increased depression

The same may be said of the other diffusible stimulants, such as ether, ammonia, and sal-volatile. Ether injections are sometimes given while the patient is under ether anæsthesia, a proceeding which is hardly rational.

In the milder forms of shock it is possible that recovery is hastened by the use of these drugs; but even that is doubtful, and their use in severe forms of shock is certainly harmful. Caffeine acts more directly on the heart muscle, *causing it to beat more forcibly* and so bringing about a rise in blood-pressure; but its effect is temporary and is probably of little value in the severer forms of shock, whilst *in the slighter forms* it is unnecessary.

(6) **Peripheral vaso-constrictors.**—The use of drugs which cause vaso-constriction by peripheral action on the muscular coats

of the arteries has been advocated in the treatment of shock as a means of raising the blood-pressure without stimulating the central nervous system. *Adrenalin* (the extract of the medulla of the supra-renal gland) causes a marked vaso-constriction in the healthy and in the shocked animal, and its action is apparent in an animal whose central nervous system has been destroyed by pithing. It has, however, little value if given by subcutaneous or intramuscular injection, especially when shock is present, and, if used, it should always be given intravenously.

Its value is discounted by its transitory effects, for it is rapidly oxidized by the tissues and the rise of blood-pressure only lasts for a few minutes after a therapeutic injection. It is therefore best given by continuous venous infusion in dilute solution (1 : 50,000, 1 : 100,000) with warm normal saline, and will then tend continuously to raise the blood-pressure. The toxic effects, if it is given in minute doses, are negligible.

Pituitrin (the extract of the posterior lobe of the pituitary body) causes a marked vaso-constriction by peripheral action, and the vaso-constriction lasts for a much longer time after a single injection than in the case of adrenalin, so that the drug need not be given repeatedly.

As to other drugs, *ergot* and *ergotin* are found to cause a general rise of blood-pressure by peripheral action on the muscular coats of the arteries, and they are of some value in the treatment of shock; but the pressure is not maintained and their effect is much less on the shocked than on the normal animal.

None of these drugs can replace the infusion of fluid into the circulation.

(7) Administration of saline fluid.—The method which has been most largely used of late years is the injection of hot (105°–110° F.) normal saline fluid, with the object of raising the blood-pressure by filling the vascular system with fluid. Saline fluid may be administered (*a*) by the rectum, either by running into the rectum one or two pints of the fluid by means of a catheter and funnel, or by continuous rectal injection at the rate of about one pint per hour; (*b*) by subcutaneous injection, one or two pints of the fluid being injected into loose connective tissue either under the breasts in females or into the axillæ and groins of males, or the fluid may be given continuously into the subcutaneous tissue of the thighs, about half a pint being injected each hour; (*c*) by intravenous injection, one to three pints being injected into a vein, usually the median basilic of the left arm.

In considering the value of this method of treatment, it is necessary to divide the cases of shock into those in which a large amount of fluid has been lost to the body, either by hæmorrhage or persistent vomiting, sweating, or diarrhœa, and those cases in which such a

loss has not taken place to any extent. The blood-pressure (which may be taken as the measure of the amount of shock) depends partly on the amount of fluid in the vessels, and although the adjusted mechanism of the muscular coats of the arteries and veins can compensate for the loss of a considerable amount of blood and the blood-pressure remain constant, yet a limit is reached at which the blood-pressure can no longer be maintained owing to the lack of fluid. The injection of saline fluid into the empty vessels will raise the blood-pressure at once, and the immediate effect is wholly good, the heart beating more forcibly and the pulse showing a corresponding increase in strength and volume. Two or three pints should be injected into a vein, and as the blood-pressure rises the pulse becomes fuller and stronger, and a general improvement in the patient is noticed. Unfortunately, however, exudation of the saline fluid into the surrounding tissues soon commences, and this exudation progressively empties the vascular system, the blood-pressure falls, and the pulse again becomes small and feeble. A further injection can be given, and the blood-pressure again raised, and the time so gained may tide the patient over a period of shock which otherwise would have been fatal. If the case is not of great urgency, continuous subcutaneous injection of normal saline, especially if combined with adrenalin, is better than injection of a large quantity, for, although the effect is slower and not so marked, the pressure is maintained for a longer period, and so more time is gained. It is obvious, of course, that saline injection in order to raise the blood-pressure must not be made use of until all hæmorrhage has been securely arrested.

In those cases in which loss of fluid either has not occurred or is insignificant the case is entirely different. The blood has not left the body, but has accumulated on the capillary and the venous side of the vascular system, and the blood-pressure falls, not because the vascular system as a whole is empty, but because the blood is lost to the effective circulation, and as a consequence the arteries are empty. Intravenous injection is of value in giving the heart something to work upon and dislodging the accumulated blood from the capillaries and restoring it to the effective circulation. But it must be remembered that in these cases excessive injection of saline fluid into the venous system may still further embarrass the circulation, and the consequent exudation may add to the œdema of the surrounding tissue, and no good, but only harm, will result. There can be little doubt that, in many cases of shock, patients who would otherwise have recovered have been killed by the further embarrassment of the circulation caused by a sudden large injection of saline fluid. The heart and tissues have been drowned.

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(9) Mechanical pressure.—The use of mechanical compression of the peripheral vessels, especially those of the limbs, in order to maintain the blood-pressure, is also due to the researches of Crile, who claims that it provides an artificial peripheral resistance without side effects. The patient is enclosed in a pneumatic suit made of a double layer of indiarubber, which can be inflated by means of an ordinary bicycle pump When the pressure is raised by forcing air into the suit it exerts a uniform pressure over the body surface, constituting an artificial peripheral resistance, which causes a rise in blood-pressure The suit is so made and arranged that the pressure can be raised in one or all the limbs, or on the abdomen especially, and the exit tubes are so valved that the pressure can be gradually lowered as the patient recovers. By means of this suit Crile claims that he gets a control over the blood-pressure within a range of 25 to 60 mm. of mercury. This apparatus has been used both during

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In those cases in which loss of fluid either has not occurred or is insignificant the case is entirely different. The blood has not left the body, but has accumulated on the capillary and the venous side of the vascular system, and the blood-pressure falls, not because the vascular system as a whole is empty, but because the blood is lost to the effective circulation, and as a consequence the arteries are empty. Intravenous injection is of value in giving the heart something to work upon and dislodging the accumulated blood from the capillaries and restoring it to the effective circulation. But it must be remembered that in these cases excessive injection of saline fluid into the venous system may still further embarrass the circulation, and the consequent exudation may add to the œdema of the surrounding tissue, and no good, but only harm, will result. There can be little doubt that, in many cases of shock, patients who would otherwise have recovered have been killed by the further embarrassment of the circulation caused by a sudden large injection of saline fluid. The heart and tissues have been drowned.

With the idea of retaining the saline fluid in the blood-vessels, and

also of attracting water from the tissues by osmotic pressure, *gum acacia* (6 per cent. in normal saline, Bayliss) has been added to the saline solution. It is extremely doubtful, as is noted under Hæmorrhage (p. 337), whether this is more efficacious than normal saline, and as it has special dangers of its own its use is not advocated.

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severe operations on the head and neck, where shock was expected, and in the treatment of shock after operations, and good results are claimed. It may be considered a useful adjunct in the treatment of shock, but its limitations are obvious.

OPERATIONS DURING THE PERIOD OF SHOCK AFTER ACCIDENTS

It may be stated as a general rule that no operation (this usually means amputation) should be performed while the patient is in a condition of severe shock. As has already been stated, the treatment of shock is rest and warmth till the patient recovers, and the superimposition of operative shock upon the shock of an accident *is bad surgery; if the patient recovers, he does so not on account* of treatment, but in spite of it. If hæmorrhage is occurring, it must, of course, be arrested at once and as quickly as possible, by simply ligaturing the tissues *en masse,* without special care to isolate the blood-vessels. If this arrest of hæmorrhage requires an anæsthetic—it rarely does—a few breaths of ether should be given and the vessels either quickly tied or simply closed with hæmostatic forceps. The patient should be made as warm and comfortable as possible, the wound being well covered with an aseptic or antiseptic gauze dressing and lightly bandaged.

Pain, which is one of the causes of shock and of its maintenance, should be relieved by an injection of morphia, or by blocking the main nerve-trunks which lead from the injured part by injection of novocain, or by a combination of the two methods.

If much blood has been lost, two or three pints of hot saline fluid should be injected into a vein, or it may be run slowly into the rectum or *subcutaneous tissue* Direct *transfusion may* also be used if a donor can be obtained and the surgeon is skilled in the method. In *those cases in which a part is almost severed and is only attached* to the rest of the body by a few strands of tissue, it is permissible to remove it, but no attempt should be made to clean the part or fashion a stump while the patient is still in the condition of shock.

The patient must be most carefully watched, especially as regards the fullness, regularity, and tension of the pulse, and no further operation should be performed until the blood-pressure is well maintained.

In the case of a severe *accident it will usually be from six to twelve* hours before it will be safe to amputate, and no attempt should be made to hurry the time of operating, in spite of the frequent urgent *appeals of the patient's friends.* The amputation may be done under spinal or local anæsthesia, but the most satisfactory anæsthetic is nitrous-oxide gas and oxygen mixture.

Exceptions to the rule of not operating during the condition of shock are numerous, as in many accidents and diseases delay is most dangerous. For example, if an accident causes severe internal hæmorrhage, such as that following rupture of the spleen, immediate operation is indicated to stop the hæmorrhage, which otherwise may prove fatal; and the same rule holds good for accidental rupture of a hollow viscus such as the stomach, or perforation of a gastric or intestinal ulcer. Delay in these cases means the onset of general peritonitis, and the sooner the rent in the viscus is closed and the peritoneum cleaned and drained, the greater will obviously be the patient's chance of recovery.

During the period that must elapse between diagnosis and operation the treatment for shock, as described above (p. 353 *et seq.*), should be carried out.

Delay is also dangerous in cases of depressed fracture of the skull with symptoms, or in intracranial or intraspinal hæmorrhage, therefore trephining or laminectomy should be done at once and the compression relieved. The treatment of shock should be carried out during and after the operation.

In cases of secondary shock also, if it is agreed that toxic absorption taking place from the damaged muscles is an important factor in its causation, an early amputation, if possible, is advisable to limit the amount of histamine absorbed. If early amputation cannot be performed, the application of a tourniquet above the damaged muscles may limit the absorption of the toxin.

DELIRIUM

Delirium occurring after accidents and operations may be divided into four varieties, according to the cause:—

1. Delirium nervosum, or traumatic delirium.
2. Toxic delirium.
3. Delirium tremens.
4. Delirium after head injuries

Not infrequently two or more of these causes are *present in the* same case with a corresponding increase in the severity and duration of the delirium.

1. Traumatic delirium, or delirium nervosum.—This is a rather uncommon condition after operation or accident which occurs in patients with congenital or acquired instability of nervous equilibrium. The congenital cases usually have a family history of insanity, epilepsy, or eccentricity, and are themselves often neurotic or hysterical, while the most frequent of the acquired predisposing causes are chronic alcoholism, sexual excess, or senility.

The condition may follow any operation or accident, *especially if* an operation has been dreaded; and it is most frequently seen after operations on the genitalia of both males and females. It does not necessarily follow operations on the ovaries and testes more than on the accessory genital organs, although operations on these glands have an adverse psychical effect. *During the surgical period when* the chronically enlarged prostate was treated by the operation of double orchidectomy, cases of delirium and insanity *following were* common—as many as 10 per cent., according to one author—but this severe operation was always performed on elderly, often senile men, a condition which probably had more to do with the delirium than the operation itself. A more instructive example was that of a Jewish lad of 19, who immediately after an operation for a varicocele developed acute mania, for which he had ultimately to be confined in an asylum.

The delirium may be of a maniacal type, as in the above case, but in elderly people it is more often a low muttering delirium, or in some cases it may be melancholia. It most commonly appears a day or two after the injury or operation, but it may be met with as soon as the patient has recovered from the anæsthetic.

The **prognosis** *of this form of delirium is good, for the condition* usually passes off in a few days, or even in a few hours, though in other cases the delirium may continue and pass on into chronic insanity or dementia.

The **treatment** is similar to that of any other form of delirium, and consists chiefly in good nursing, good hygienic conditions, and sedatives if necessary.

2. ***Toxic delirium.***—This form of delirium, as its name implies, is due to the absorption of poison from a wound. In the majority of cases the poison is produced by the infective bacteria, especially the pyogenetic forms, but it may be due to the absorption of certain chemicals, such as iodoform, used in the dressing, or from the administration of *chloroform* or *morphia*.

The variety due to absorption of the toxins of the *pyogenetic bacteria* usually occurs on the third to the fifth day after the operation or accident, and is associated with rise of temperature, general malaise, and other symptoms of toxic absorption. The delirium at first is usually of the active, *restless type, with increased pulse-rate, constant* talking, and sleeplessness, the delirium being most marked at night; *but if the absorption continues*, the patient passes into an asthenic state with low muttering delirium and picking at the bedclothes. This condition, the so-called "typhoid state," is sometimes seen from the first in cases of severe intoxication—*for example, that associated* with infection with the bacillus of malignant œdema—or in elderly and *debilitated patients*.

In cases of *iodoform poisoning* there is at first a period of excitement with hallucinations, and refusal to take food, followed by a period of depression, which in fatal cases deepens into loss of consciousness, coma, and death.

The first indication for **treatment** in the infective variety is to give free exit to the toxic material, so that absorption may cease; if this can be done the delirium soon passes off. The further treatment, both general and local, is that of an infected wound, sedatives being given, if considered necessary, to secure rest and sleep.

In iodoform poisoning the use of the drug must be stopped immediately, but this is not always followed by amelioration of the symptoms, and death has occurred twenty-nine days after their onset, although the application of the drug was discontinued at once.

3. **Delirium tremens.**—This form of delirium is always associated with chronic alcoholism, although the exciting cause is often a severe trauma such as a fracture or operation, or an acute illness such as pneumonia. The condition is sometimes seen in children to whom small quantities of alcohol have been given, and it not infrequently occurs in adults who have rarely been intoxicated but who are addicted to the use of alcohol in frequent small doses The diagnosis often comes as a complete surprise and is received with incredulity by the relatives who may have been living with the patient. It is a matter of dispute whether the sudden stoppage of alcohol in a patient who is addicted to its use plays any part in the causation of the condition, and most authorities deny such stoppage any etiological significance, but it may be inadvisable to interdict alcohol to a patient accustomed to it, just after an operation or accident, on account of the general restlessness and discomfort that may result.

Delirium tremens is an excited or motor melancholia connected with hallucinations, delusions of persecution, mental depression, often suicidal tendencies, and loss of concentration of attention. The symptoms usually begin a day or so after the operation or accident, and develop gradually. The prodromal symptoms are sleeplessness, restlessness, and constant talking, often incoherent, although the patient will give sensible answers to questions The temperature is usually raised (100° F.), the tongue furred, the bowels are constipated, and the lips and fingers tremulous. The appetite is poor, and there may be absolute disgust for food, but the patient is usually thirsty and drinks large quantities. These symptoms are indicative of the onset of an attack of delirium tremens, and if the patient can be induced to sleep and take food the condition may pass off.

The next stage of the disease is one of extreme restlessness, incoherency, and hallucinations These hallucinations are usually of sight, the patient seeing animals of any description and making attempts

to brush them away or to escape from them. Hallucinations of hearing are also common, the patient complaining of voices which threaten him, and often holding long, incoherent conversations with imaginary persons. He may also complain of attempts to injure him, and may do himself serious damage in his attempts to escape from his persecutors. Insensibility to pain is a marked feature of these cases, so that the patient will remove his splints and attempt to walk on a fractured limb without showing any signs of pain.

The physical changes are no less pronounced than the mental; the pulse is rapid and feeble; there is complete loss of appetite and digestive power, with a rapid loss of flesh and strength. Constipation is the rule, but there may be diarrhœa, and the urine and fæces are usually passed into the bed.

The patient insensibly passes into the third stage—that of exhaustion, with a sleepless, low, muttering delirium, rapid feeble pulse, dry furred tongue, sordes on the lips, and a falling temperature; and, if the condition be not relieved, death from exhaustion follows.

The **prognosis** of delirium tremens is good in a first attack occurring in a fairly healthy young subject; but in elderly people, after one or more attacks, the prognosis is grave, and death may suddenly take place from heart-failure.

Complete mental recovery, so far as the condition of chronic alcoholism will allow, is the rule after a first attack; but the hallucinations or delusions may persist and the condition pass into one of delusional insanity or dementia.

Treatment.—The great indications for treatment during the prodromal stage of the disease are to get the patient to sleep naturally and to take food. Plenty of fresh air in the room, easily digested ... and night, tepid spong- ... ndition allow it, exercise ... chance of a natural sleep and may avert the attack. The bowels should be opened with a brisk purge and the patient not allowed to get constipated again. Alcohol, especially a malt liquor (stout), is often prescribed as a sedative on the assumption that sudden cessation of all alcohol is a cause of the condition, but its value is doubtful; and if it be absolutely necessary to give hypnotics, paraldehyde, morphia, bromide, or chloral is preferable on account of the more certain action of these drugs. The majority of them are cardiac depressants, and in a disease in which the chief cause of a fatal result is heart-failure their action must be carefully watched. Paraldehyde is the drug most largely used for procuring sleep, as it has only a slight action on the heart.

During the stage of actual delirium the patient must be most carefully watched, for he may exhibit homicidal and suicidal tendencies,

or in attempting to escape from imaginary enemies he may fail to recognize pain and danger and may seriously injure himself.

The use of stimulants during the early stages of delirium tremens is a matter on which there is a difference of opinion, some surgeons withholding them entirely, whilst others advocate their use, especially in the form of alcohol or strychnine. In the younger and more robust patients stimulants are unnecessary, and in elderly patients early stimulation is followed later by depression, and harm probably results; but in the stage of exhaustion their timely use may tide the patient over a critical period. Even then more reliance should be placed on careful and frequent feeding, good hygiene, rest, and quiet.

Physical restraint in cases where it is necessary is best carried out by firmly securing the patient in bed by mechanical means so arranged that he cannot injure himself. The patient will often recognize the futility of resistance, while struggling with an attendant will increase the excitement and bring with it a corresponding danger of sudden heart failure.

4. **Delirium after injuries to the brain.**—After injury to the brain any one of the above described conditions of delirium may occur if the cause be present; but the injury to the brain itself may be the direct cause of the delirium. The condition usually depends on laceration of the brain, and particularly laceration of the frontal lobes, and is spoken of as cerebral irritation. The state is one of extreme mental irritability with physical depression, and may end in lunacy, although only about ½ of 1 per cent. of insanity cases can be traced to injuries of the head.

FEVER

Fever—that is, rise of temperature, with general malaise, occurring after an operation or accident—may be divided into three varieties, according to the cause, as follows:—

1. Aseptic traumatic fever.
2. Infective fevers.
3. Fever in connexion with injuries to the brain and cord.

1. **Aseptic traumatic fever.**—Within twenty-four hours of an operation or accident in which thorough drainage of the wound has not been employed, or in which blood is extravasated into the tissues, it will be found that the patient's temperature is above normal and that he complains of headache, loss of appetite, and malaise (Chart 2). This rise of temperature and malaise are due to an absorption into the blood, from the wound, of certain substances which free drainage would carry into the dressing. It is believed that the fever is due to the absorption of ferments, of which the most important is fibrin

ferment, found in the extravasated blood and serum. This ferment has been demonstrated free in the blood after an injury, and injection of it is found to be followed by a rise of temperature. Other ferments producing the same effect are pepsin and pancreatin and solution of *hæmoglobin*.

Aseptic traumatic fever is most marked if the tissues have been badly bruised and lacerated, or if strong antiseptics have been used. These conditions cause the blood-vessels to pour out more inflamma-

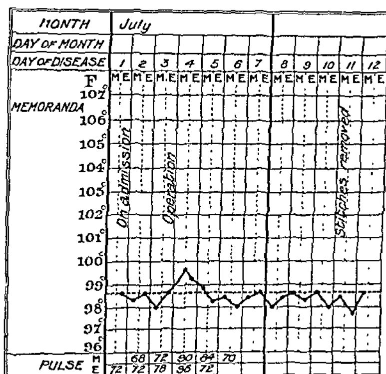


Chart 2.—Case of aseptic traumatic fever following operation. The wound healed by first intention.

tory lymph, which, if not carried off by drainage, has to be absorbed, with corresponding *rise of temperature*. The temperature rarely exceeds 100° F., except in the case of children, and usually falls to normal in forty-eight hours, although the rise may be continued longer if the amount of serum to be absorbed is large. With the fall of temperature the other symptoms disappear. A continuance of the fever may be associated with *constipation after an operation, and be due to absorption* of soluble decomposing substances from the alimentary canal.

A subject of chronic malaria may have a rise of temperature some hours after operation.

Aseptic traumatic fever requires no special *treatment* and may be considered almost physiological. An aperient and a suitable regulation of the diet after an operation are all that is needed. In those cases in which suppuration occurs, the condition passes into that of septic traumatic fever.

2. **Infective fevers.**—An infective fever is caused by the growth in wounds of various micro-organisms and the absorption into the blood of their products of metabolism. These organisms may be

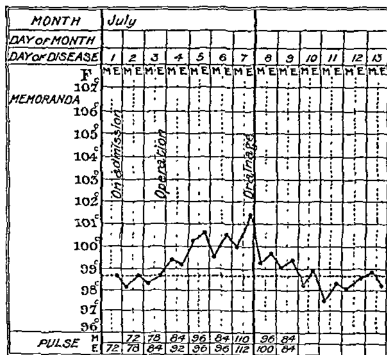


Chart 3.—Case of septic traumatic fever following operation.

divided into two great groups—the specific, causing specific infectious fevers, and the non-specific. The *non-specific* are the common organisms of suppuration, such as staphylococcus, streptococcus, and B. pyocyaneus and the symptoms caused by the absorption of their toxins are grouped under the term of infective traumatic fever or, more simply, sepsis. Should the organisms themselves invade the blood-stream and give rise to secondary metabolic inflammatory foci, the condition is spoken of as septico-pyæmia.

Infective traumatic fever, or sepsis.—The rise of temperature in this condition may occur at any time after the infliction of a wound, depending on the time of infection and the virulence and

incubation period of the organism. In ordinary cases the fever is well marked on the third day after the operation, aseptic traumatic fever gradually merging into the more serious condition (Chart 3).

The patient shows a rise of temperature to 102°–104° F., or the onset may be marked by a rigor in an adult and a convulsion in a child. The other symptoms are quickened pulse- and respiration-rate, constipation or diarrhœa, and loss of appetite and digestive power.

The urine is scanty, high-coloured, and loaded with urates, and it may be albuminous. The skin is hot, dry, and flushed, and there is often mental disturbance and delirium. If the process continues, there are rapid loss of body weight, muscular weakness, and a secondary anæmia due to hæmolysis. If the wound be inspected, the edges will be found acutely inflamed and there will be tension of the stitches. The surrounding tissue is red, œdematous, and painful, while the patient complains of a throbbing pain in the wound, and if the edges are separated pus will probably exude. Free drainage will probably be followed by a fall of temperature and a cessation of the symptoms.

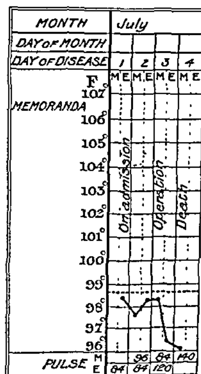


Chart 4.—Case of death from shock after operation.

In cases where either a large area has been infected, or the virulence of the organism is very great, the temperature high, and the symptoms very severe, or in elderly people or those debilitated from any other cause, there may be rapid cardiac failure without rise of temperature (Chart 4). These are spoken of as cases of septic intoxication, and they frequently end in death, an excellent example being the acute infection of the placental site which occurs after confinement—the so-called puerperal fever.

Another form of the same variety of fever occurs when it is impossible to drain a septic focus efficiently, as when suppuration occurs in bones, and there is a constant slight absorption of toxins taking place over a long period.

The temperature in these cases is usually intermittent, with an

evening rise, and there is progressive muscular weakness, with emaciation, hæmolysis, cardiac weakness, and other symptoms of toxæmia. Should the process continue the patient may die of exhaustion, or lardaceous degeneration of the smaller arteries may occur. Such cases are sometimes spoken of as examples of hectic fever, but a better term is chronic sepsis.

Treatment.—The treatment of fever due to wound infection is largely the treatment of the wound. The products of bacterial activity must be carried away from the wound by free drainage, and if necessary by incisions into the surrounding tissue.

In cases of septic intoxication due to absorption from a large cavity, this must be thoroughly washed out with antiseptic lotion. Cases of chronic sepsis should be treated by removal of necrosed tissue and free drainage, or in some cases amputation may be necessary.

The treatment of the toxæmia due to the toxins already absorbed is appropriate serum-therapy.

During the continuation of the fever the diet should be light and nutritious, the bowels should be kept open, and fluid should be freely given to aid the excretion of the toxins by the kidneys. In chronic cases fresh air and sunlight are of the utmost importance; many patients treated in towns fail to improve, but do so if sent to the seaside or the country.

There is rarely any need for specific medication to reduce the temperature, and probably antipyretics do harm rather than good; but if the temperature be very high and these remedies be not otherwise contra-indicated, cold or tepid sponging or baths should be used to reduce the temperature, and will improve the pulse, respiration, and physical functions.

Specific infectious fevers.—As far as the rise of temperature and general constitutional disturbance are concerned, the specific infectious fevers do not differ greatly from the non-specific, the difference in the two conditions being the presence in the former of specific symptoms, both local and general.

The same applies to the *treatment* of the fever, the general treatment being that given above for the non-specific fevers, while the specific treatment consists of appropriate serum-therapy and means to counteract the specific symptoms, such as the muscular spasms in tetanus.

In chronic specific infectious fevers, such as tuberculosis, fresh air, sunshine, and good hygienic conditions are at least as important as specific treatment, and are necessary, whether vaccine treatment is used or not.

3. Fever associated with brain and cord lesions.—A rise of temperature, sometimes very marked, may be met with after various lesions of the brain and spinal cord. The best instance

of this rise of temperature is met with after hæmorrhage into the pons Varolii, when the temperature may rise to 105°–107° F., the condition being usually associated with pin-point pupils. After any cerebral injury with hæmorrhage and compression the temperature may be raised, and a steady rise of temperature frequently precedes death from acute cerebral compression.

The explanation given of this rise of temperature is that it is due to interference with the thermogenetic centres, causing either increased metabolism, which raises the temperature of the body generally, or diminished loss of heat by irradiation as a result of lessened rapidity of circulation.

Rise of temperature may also be found during mental excitement and in hysterical states, probably due to functional disturbance of the heat centres.

Treatment.—The treatment of this rise of temperature is the treatment of the underlying condition, and, as a rule, little can be done. In cases of cerebral compression the compression may be relieved by trephining, and the temperature falls; but a rise in temperature after brain injury is a grave prognostic sign.

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TOXÆMIA, SEPTICÆMIA, PYÆMIA

By E. K. MARTIN, M.S., F.R.C.S.

TOXÆMIA

Definition.—The current conception of the term toxæmia implies the presence in the blood of poisons which result either from disturbances of metabolism or from microbic activity. For the purpose of this article the former variety will be excluded and the latter limited to the micro-organisms concerned in suppuration. When pathogenetic bacteria are growing in any of the tissues of the body the products of their metabolic activity are absorbed into the circulation and produce certain morbid changes in the cells of the organs and tissues. These changes have their clinical expression in a relatively constant series of constitutional symptoms, which show but little specific relation to the variety of micro-organism concerned.

Morbid anatomy.—The blood is watery and presents the characteristic appearance of a secondary anæmia. Owing to destruction of the red cells, hæmoglobin is set free and becomes dissolved in the plasma. It stains the lining endothelium of the heart and great vessels and, after chemical alteration, produces an icteric tinge in the skin and mucous membranes (hæmolytic jaundice). The white cells are increased in number, chiefly by addition to the polymorphonuclear element.

The heart is often moderately dilated, with cloudy swelling or fatty change in its walls The great vessels show no special alteration, but damage to the walls of the capillaries may be indicated by petechial hæmorrhages in the skin, in the mucous and serous membranes, beneath the endothelial lining of the heart and, occasionally, in the substance of solid organs.

The lungs are congested, may be œdematous, and often contain irregular patches of consolidation (broncho-pneumonia) The spleen is moderately enlarged, soft, and congested to a deep plum colour. The liver and kidneys are congested, and show fatty degeneration. Microscopically, the glomeruli of the kidney often appear damaged by exudation and hæmorrhage. If diarrhœa has been a feature of the case the intestines are congested and may present superficia ulceration of the mucous membrane.

Clinical picture.—The chief subjective symptoms of toxæmia are a feeling of illness, loss of desire or actual distaste for food, headache, and a restlessness which betrays itself as inability to find a comfortable position during the day or to sleep for any length of time at night. Thirst is the rule, but, at times, refusal to take sufficient fluids may accompany anorexia.

Among the more constant of the objective signs of toxæmia resulting from focal suppuration is pyrexia. The rise of temperature may be gradual or abrupt. In the latter case there is often an initial rigor. The normal diurnal variation is exaggerated, with an evening rise to 103° or 104° Fahr. and a morning fall to between 99° and 100° Fahr. ("hectic fever"). Occasionally the variation is still greater and ranges [illegible] to 2 or 3 degrees below. The [illegible] and in the case of localized [illegible] 100. The pulse at first is regular, full and bounding, but with continuance of the toxæmia it becomes smaller, more rapid and less regular.

The skin at first is hot and dry; later, sweating may be profuse, independently of rigors, and a sweat rash is often seen. At the onset the face is flushed, but with the progress of hæmolysis pallor succeeds the flush and a yellow tinge appears. The tongue is dry and coated with a white fur; later it becomes brown and cracked, or red and shiny, and sordes appear on the lips.

Vomiting is frequent at the beginning, but does not usually persist, though it may appear again as an accompaniment of the offensive diarrhœa which is so often present in long-continued sepsis.

The urine is scanty and high-coloured, and the damage to the kidney is generally indicated by the presence of albumin. A few hyaline casts may be found. Blood, with albumin and casts in considerable quantity, is only present if an acute nephritis has developed.

With increase in the duration or intensity of toxæmia there is progressive weakness, and loss of flesh The patient loses interest in his surroundings, tends to slip down in the bed, and may have difficulty in swallowing. The hands and tongue become tremulous. Sleep may be accompanied by wild and terrifying dreams, and a nocturnal delirium appears.

Amyloid infiltration (*lardaceous or waxy disease*)—In patients who have suffered from a long-continued toxæmia due to absorption from a suppurating focus, there may be found at autopsy deposits of a firm, translucent substance in the viscera, particularly in the liver, spleen and kidneys. This amyloid substance (lardacein) is deposited around the walls of the capillaries and fills the spaces between their endothelial lining and the specific cells of the organ, and it is also found in the walls of arterioles and veins. It stains dark brown with

solutions of iodine, and gives a metachromatic reaction to various aniline dyes, i.e. it stains a different colour from that of the remainder of the infiltrated organ (thus, with methyl-green it shows red against the general green of the tissues).

During life, amyloid infiltration produces a firm enlargement of the liver and spleen, and, owing to its deposition in the glomeruli of the kidney, leads to the appearance of amyloid casts in the urine.

Chemically, amyloid substance is a protein, but its exact composition is neither known nor certainly constant

Treatment.—Since toxæmia is a general manifestation of absorption from a local infection, surgical removal of the influence of the primary focus by drainage, ablation, or sterilization constitutes the fundamental basis of its treatment. Methods of combating the constitutional symptoms of the condition are discussed in connexion with septicæmia (*see* p. 373).

SEPTICÆMIA (BACTERIÆMIA)

Definition.—The term septicæmia denotes the presence of living, pathogenetic micro-organisms in the circulating blood. The existence of the condition can only be established by the cultivation of such an organism from blood withdrawn during life. Its symptoms are due to the coincident toxæmia. Since many diseases, e.g. generalized tuberculosis, infective endocarditis, acute specific fevers such as pneumonia, typhoid fever, etc., fall within the definition of septicæmia, this term will here be restricted to cases in which pyogenetic organisms have invaded the blood-stream

The conditions under which pathogenetic organisms gain access to the circulation are not sufficiently clear to allow of precise statement. In general terms, the two factors involved are the attacking power of the organism and the resistance of the patient, the former including the virulence of the particular strain present and its numerical concentration at the primary focus of infection.

Varieties.—Owing to the variation in type of septicæmia as met with in surgical practice, no single basis of classification is adequate to include all lines of approach to a clinical comprehension of the condition. Logical classification is based upon the variety of organism isolated from the blood—streptococcus, staphylococcus, etc.; but associated with this, and in no way conflicting with it, is the clinical grouping into septicæmia appearing as a terminal accompaniment of overwhelming and fatal sepsis, septicæmia appearing as a temporary incident consequent upon the presence of an imperfectly drained focus of infection, and septicæmia which has become so established as to constitute the main aspect of the disease.

Etiology.—The organisms most commonly found in septicæmia are the streptococcus (about 50 per cent. of all cases), staphylococcus, pneumococcus, B. coli, and B. pyocyaneus. Less common are those associated with special types of infection, e.g. gonococcus, B. anthracis, and B. aerogenes capsulatus. The last-named organism, like other anaerobes, is rarely met with as a cause of septicæmia in civil practice, but during the war was not uncommonly found associated with a hæmolytic streptococcus in the terminal blood infections preceding death from infected wounds.

The portal of entry of organisms into the blood-stream is usually a focus of suppuration, the drainage of which, from anatomical or other reasons, is inadequate. Occasionally all evidence of the point of origin is wanting, and in such cases an absence of resistance on the part of the patient to the organism involved must be assumed. Such specialized lowering of resistance appears to be compatible with otherwise full physical vigour.

Pathology.—The post-mortem appearances of a case in which death has been preceded by septicæmia are in no way indicative of the presence of organisms in the blood, because the changes in the tissues are due to toxins produced by the bacteria, and it is immaterial to the final picture whether these are multiplying without or within the circulatory system. The tissue changes are therefore those of severe toxæmia (*see* p. 369).

Clinical picture.—1. Terminal septicæmia.—Towards the end of a fatal illness of pyogenetic origin the onset of septicæmia is usually indicated by a rapidly progressive increase in the pre-existing toxæmia, occasionally by a definite rigor. The characteristic appearance of the temperature chart is a parallel rise of both morning and evening records, though in some cases the terminal rise is continuous and shows no remission. A height of 104° or 105° F. is common, but in the most severe cases the temperature reaction is on a lower scale.

The pulse increases to 120–140, and can usually be counted at the wrist almost until the last. The heart becomes dilated. The face is at first flushed, the eyes are bright, the tongue is dry or glazed, and sordes appear on the lips. Later, hæmolysis is indicated by progressive pallor and the appearance of a yellow tinge in the skin and conjunctiva. Petechial hæmorrhages may occur.

Usually, but not necessarily, the patient feels ill and loses appetite. Often he suffers severely from headache and, at an early stage, becomes delirious and noisy at night. With the increase of toxæmia the period of delirium gradually encroaches on that of consciousness, the patient becomes more and more quiet and frequently dies in coma. The fingers and tongue are usually tremulous. The degree of thirst

is dependent on the amount of sweating, which may be profuse. The urine is scanty and contains albumin. Diarrhœa, with its accompaniment of abdominal distension, and hiccup are often both intractable and distressing.

2. Temporary septicæmia.—Whenever, on account of delay or inadequacy in operative intervention or of difficulty of anatomic access, drainage of a suppurating focus is or becomes insufficient to allow bacteria to escape as fast as they multiply, a " head " of organisms may be established sufficient to determine their escape into the blood stream. If now, in the presence of a positive blood-culture, the focus of infection be freely opened by incision or removed by amputation, the blood often becomes sterile in a few days. It is then clear that the resistance of the patient is adequate to deal with the organism which has gained access to the circulation, provided that the " feed " from the primary focus of infection does not transgress definite limits of intensity and rate.

The onset of a temporary septicæmia and its relief by drainage are reflected on the temperature chart and in the symptoms in logical correlation with the results of bacteriological examination of the blood.

3. Established septicæmia.—When a state of septicæmia persists after drainage or removal of the primary focus of infection, or arises from a trivial or unidentified primary focus, it may be assumed that the patient is deficient in resistance to the organism which is found in the blood. The septicæmia may then be termed established. In contradistinction to the terminal and temporary varieties of septicæmia where the symptoms of the blood infection form incidental additions to the symptoms of the original disease, an established septicæmia provides the sole or dominating element in the clinical picture.

The patient in whom septicæmia develops in consequence of an ordinarily negligible injury is often vigorous and in apparently full physiological health. The term health is here used in its conventional sense of physical fitness, which does not include the conception of immunity from invasion by pathogenetic organisms. Such immunity is conferred mainly by that specific inoculation with minimal doses which is a normal incident of daily life and without which health, though rude, is relative. In a person who has been for some time out of contact with pyogenetic organisms, e g. on a holiday, the most robust health is consistent with inadequate resistance to the streptococcus.

When septicæmia arises from an apparently trivial wound the organism found in the blood is usually the streptococcus, introduced from without by the agent which causes the breach in the skin. The

mode of origin of staphylococcal septicæmia is, in general, less demonstrably direct The primary focus is usually some minor lesion of the skin, such as a boil, scratch, or patch of impetigo, from which a potential escape into the blood-stream may be presumed. Owing to the freedom of drainage of cutaneous lesions a condition of septicæmia is not likely to become established except through the formation of a secondary focus of infection in some part which, by reason of its depth from the surface and of the structural conformation of its constituent tissue, affords the conditions necessary to development of the requisite " head " of organisms. The tissue which best fulfils these conditions is bone, the precise point at which the secondary focus of infection arises being often determined by mechanical violence of otherwise minor importance. Once such a focus is established, the local multiplication of bacteria is so rapid, and their escape from the rigid confines of an undrained bone so difficult, that determination of whether the septicæmia is coincident with or consecutive to the clinical appearance of osteo-myelitis may be impossible. That the septicæmia is frequently secondary to the development of suppuration within the bone is, however, suggested by those fatal cases of osteo-myelitis in which a terminal septicæmia precedes death.

In the acute form of the disease the symptoms do not differ from those described above as characteristic of terminal septicæmia. In the more chronic forms the symptoms differ only in degree.

Diagnosis.—Examination of the blood in septicæmia should be planned on an adequate scale, not less than 10 c.c. being withdrawn and diluted with enough (100 c.c.) of the medium employed to obviate bactericidal action of the serum. The organism is not necessarily present in every sample and, in the event of a negative finding, the examination should be repeated if there is strong clinical presumption of the existence of the condition. In view of the technical difficulty of avoiding skin contamination, a higher degree of scepticism is advisable in accepting the presence of the staphylococcus in the blood, particularly if the organism is Staphylococcus albus, than is necessary in the case of the streptococcus. The red-cell count is indicative of the grade of hæmolysis, but the leucocyte count is usually of little value owing to the variable factor introduced by the influence of the primary focus of infection.

Although a diagnosis of septicæmia is only justified by cultivation of micro-organisms from blood withdrawn during life, a strong presumption of its existence may often be afforded by the clinical evidence. Indications for bacteriological examination of the blood are the undue persistence or intensity of the toxæmia arising from a primary focus of disproportionate size or of a type notorious for its association with septicæmia, e.g. infection of intact or damaged bone.

Prognosis.—The outlook is always grave, but not necessarily hopeless. If a division be made between cases with an obvious, undrained, primary focus and cases in which the primary focus is negligible apart from its importance in allowing access of bacteria to the circulation, prognosis in the first group depends on the possibility of establishing adequate drainage of the primary focus. In the second group, the main factors influencing prognosis are the type and virulence of the infection and the ability of the patient to develop immunity to the particular organism present.

Treatment. Operative.—Drainage or removal by amputation of the primary focus of infection is the most important single factor in treatment, but can, of course, only be applied to cases in which an undrained focus of some magnitude exists. In infection of a limb-bone or joint, if micro-organisms are found in the blood in spite of local drainage amputation is indicated.

Bactericidal.—The injection of antibacterial serums has so far proved of little value, and in no case can benefit be expected from the employment of small doses. If used, 50 to 100 c.c. of the appropriate serum should be given daily into a vein.

Sterilization of the blood by intravenous injection of various antiseptics has naturally been attempted, but has met with little success. During the war eusol was used extensively in the treatment of streptococcal septicæmia, but any improvement obtained was temporary and could reasonably be attributed to the quantity of fluid passing through the circulation and causing a temporary increase in the rate of elimination of toxins.

Passive immunization.—In streptococcal septicæmia transfusion with whole blood produces a temporary improvement for 24–48 hours, but does not confer lasting immunity. Preliminary immunization of the donor with a vaccine prepared from the recipient has been suggested. The method is still on trial.

Active immunization.—Injection of a vaccine made from the organism found in the patient's blood may be of value in chronic septicæmia, and merits trial in all cases, both acute and chronic, in which septicæmia becomes established in spite of adequate surgical treatment of the primary focus.

General.—If conditions are favourable, the patient is best in the open air. If this is not feasible, the room should be freely ventilated. The diet may be as nourishing as the degree of anorexia allows, and the taking of fluids should be encouraged. Alcohol has no specific value, and its use will depend on the habits of the patient and the preference of the surgeon. Symptomatic treatment will be required for headache, sleeplessness, delirium, and diarrhœa.

PYÆMIA

Pyæmia differs from septicæmia in that secondary *foci of suppuration* appear spontaneously in parts distant from the primary focus, notably in the joints, in the serous cavities of the chest, and in the kidneys. In other respects the two conditions are identical, and they are here considered separately solely for convenience of classification, the distinction between them being purely clinical.

Origin of secondary abscesses.—The mode of origin of the secondary foci of suppuration can often be determined with precision, particularly when the pleura is their site. Organisms first obtain an entry to the circulation by direct spread through the wall of a vein in the neighbourhood of the primary focus of infection. An infected thrombus is formed in the inflamed vein and spreads to the main vein of the region, where it may often be seen projecting into the lumen, loosely attached to the wall Portions of this infected clot become detached from the main mass and form septic emboli which are carried by the blood-stream to the lungs, where they become arrested in the capillaries and form septic infarcts or secondary abscesses, from which, in turn, the pleura is infected. Detachment of an embolus is often signalled by sudden local pain at the site of arrest.

The mechanism of production of the secondary abscesses in pyæmia is not always capable of such accurate definition. Suppurative arthritis, a common pyæmic manifestation, is not demonstrably of embolic origin, and although it is possible to assume a small local injury which provides a nidus for the growth of organisms from the blood, such an explanation remains hypothetical. The rapid power of recovery shown by an infected joint after a single operative evacuation and closure does, however, suggest that the infection belongs to the category of a single implantation rather than to that of a constant feed of organisms from the circulation

Etiology.—In most cases of pyæmia the primary focus is an infected bone, the drainage of which is not adequate to allow free escape of organisms to the surface. Thus it is seen particularly in acute suppurative osteo-myelitis, and in sinus thrombosis following infection of the mastoid antrum or ethmoidal cells. In conformity with its usual origin in bone, the bacteria commonly found are the Streptococcus pyogenes and the Staphylococcus pyogenes aureus. The causative organism can usually be cultivated from the pus of the secondary foci. The ease with which it can be recovered from the blood depends on the intensity of the septicæmic element, and in the more chronic types of pyæmia, characterized chiefly by recurrent embolism, a state of septicæmia may never become sufficiently established to give a positive blood-culture.

Other micro-organisms which may be associated with secondary foci of suppuration are the pneumococcus, gonococcus, B. typhosus, B. coli, B. pyocyaneus, etc.

Pathology.—The distinctive pathology of pyæmia, apart from that of the coincident toxæmia, is concerned with the formation of the secondary foci of suppuration. These are usually multiple. The mode of access of organisms from primary focus to blood-stream, via local phlebitis and infection of the resultant thrombus, has already been described. In pyæmic arthritis the joint cavity is distended with pus from which the causative organism can be cultivated. Destruction of the articular surfaces is relatively slight in comparison with infection of the same duration following a penetrating wound. In infection of the serous cavities there is little tendency to the formation of limiting adhesions.

Clinical picture.—The subject of acute pyæmia is suffering from local retention of the products of infection, and therefore presents symptoms of toxæmia or septicæmia. The first sign which suggests the appearance of pyæmia is usually a series of rigors, followed at an interval of a few days by development of the characteristic secondary foci of infection. The onset of these may be heralded by local pain, but is not infrequently insidious, and hence may give rise to the apparently rapid appearance of pus in large quantity. Since definite rigors may be absent throughout, the importance of systematic daily search for secondary foci of suppuration in patients with symptoms suggestive of septicæmia can scarcely be overstated. The potential development of pyæmia is often suggested by signs of thrombosis in the main regional vein corresponding to the site of primary infection.

The recognition of secondary suppuration in the joints, subcutaneous tissue, and lungs usually presents no difficulty. Embolism of the spleen is indicated by a sudden local pain followed by tenderness and moderate enlargement. Abscesses in the kidney sometimes produce local tenderness, with blood and pus in the urine, but as they are usually small, localized, and surrounded by kidney substance showing only the changes produced by toxæmia, they may not be recognizable with certainty before autopsy. Suppurative pleurisy may develop without recognizable pulmonary embolism, and is often accompanied by pericarditis and peritonitis. Enlargement of the heart and cardiac murmurs are usually present, and do not necessarily indicate infective endocarditis, though the development of this condition should always be suspected. Embolism of the central artery of the retina produces sudden blindness, and may be followed by suppuration in the globe. Cutaneous symptoms such as jaundice, scarlatiniform rash, and petechiæ are associated with the coincident septicæmia.

Treatment.—The treatment of pyæmia, apart from that of the accompanying septicæmia, is concerned with drainage of the *secondary foci of suppuration*, wherever these are amenable to surgical intervention. Subcutaneous abscesses are incised, suppurating joints opened as soon as diagnosed, *washed out with saline or with* an unirritating antiseptic, such as flavine (1 : 1,000 normal saline) or eusol, and closed. They should be immobilized while painful, but active movement should be encouraged at the earliest possible moment. Drainage should be avoided on account of the secondary infection along the track which necessarily follows this mode of treatment.

Suppuration in the serous cavities should be treated on the general lines applicable to the same condition when arising as a primary infection.

Chronic Pyæmia.—When chronic, pyæmia is characterized by the development of abscesses in the subcutaneous tissue and intermuscular planes. The occurrence of an abscess is usually preceded by a rigor. In the intervals between the development of successive secondary foci the patient usually feels well, but looks pale and shows *a slight degree of pyrexia. The blood picture is that of secondary* anæmia. Micro-organisms are rarely present in the blood in sufficient number to give positive results from culture. The best opportunity of finding them in the blood is during a rigor. A primary focus of infection is most often found in the teeth, tonsils, nasal sinuses, middle ear or anal canal. In the treatment of chronic pyæmia, apart from removal of the primary source of infection when found, *the general hygiene of the patient is of the utmost importance.* The use of a vaccine prepared from the organism found in a secondary abscess may give good results.

Portal Pyæmia.—The primary focus of infection may be situated in any part of the territory drained by the portal vein, but in the majority of cases is in the vermiform appendix. From an infected thrombus in the appendicular veins emboli are carried to the liver, where *they initiate multiple secondary* abscesses. Suppurative thrombosis of the superior mesenteric or portal vein may occur. The onset of portal pyæmia during an attack of appendicitis is indicated by rigors, progressive anæmia, an icteric tinge, and tenderness and enlargement of the liver. The condition is commonly fatal.

TUMOURS

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AND

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A TUMOUR belongs to the group of pathological lesions which are characterized by the local new formation of tissue. This group also includes inflammatory deposits, localized hypertrophies, and supernumerary structures, from which tumours have to be distinguished. The diagnosis of a tumour, whether considered from the clinical side by the surgeon, or the morphological side by the morbid anatomist, is concerned with the discrimination between these various forms of new-tissue formation.

Confusion often arises from the unfortunate use of the term "tumour" for any condition characterized by a swelling, independently of its nature.

It is at once clear that every swelling is not a "tumour," and, further, it may be remarked that a tumour does not necessarily cause a swelling. The destruction of tissue occasioned by the growth of a tumour, together with changes in the tumour substance itself, may actually result in a diminution in the size of the affected part. For instance, a breast the seat of a cancerous growth is often smaller than the opposite healthy gland.

Of the different forms of new-tissue deposit above mentioned, there is no doubt that certain varieties of chronic inflammation present the most striking resemblances to true tumours. For instance, in the group of diseases known as the infective granulomas, and including, amongst others, tuberculosis, syphilis, leprosy, and actinomycosis, the local manifestation of the disease often takes the form of considerable tumour-like masses of granulation tissue resulting from the effect upon the tissues of a specific microbic agent. Such a granuloma may present features closely allied to those of a true tumour, and from the clinical point of view it may be stated that this resemblance is more often seen in a syphilitic gumma than in any other form of chronic inflammatory new growth. A most striking instance of the close relationship which may exist between a simple hyperplasia and

a true tumour-formation is afforded by the papillomatous outgrowths (venereal warts) which are not uncommon on the external genitalia. These growths clearly result from the irritation of discharges, and in their earlier stages they may completely disappear with the cessation of the irritation which causes them. Later, however, they may behave more like actual tumours, and present a progressive growth which is independent of the continued action of the irritant.

Further evidence of the difficulty of clearly differentiating between the tumour-formations and the hypertrophies and inflammatory hyperplasias is afforded by the fact that certain tumours, especially of the malignant type, frequently take their origin in tissues already damaged by chronic inflammation. This subject will receive further notice subsequently, and it will be seen that in the present state of our knowledge it is often impossible to decide exactly when the cell proliferation passes the limit which separates the chronic inflammation from the actual tumour.

Origin.—The origin and causation of tumours are matters of extreme interest, but unfortunately very little is definitely known concerning them. Reference will be made in the course of this article to some of the most important work which has been carried out in the attempt to solve these problems, particularly in connexion with malignant growths. For the present, it must suffice very briefly to indicate certain considerations having a bearing upon the general subject.

In some instances there is reason for supposing that the cells in which the tumour arises have come to occupy their abnormal position by a simple process of displacement in the course of embryonic development, or as a result of trauma. For instance, in view of the close relationship of the skeletal muscles with the skeleton itself, it is not difficult to conceive of the displacement at an early period of certain cells destined to become cartilage and their inclusion among the cells which become muscle-fibres. A further most striking instance of apparent displacement is met with in the origin of cartilaginous tumours of the bones in the immediate vicinity of the epiphysial cartilage, for it is easy to suppose that such a tumour develops from cartilage cells which have become detached from their normal position and, instead of taking their share in the normal growth of the bone, grow independently into a tumour. Again, the development of the kidney occurs in tissue which is closely connected with the muscle plates on either side of the vertebral column, and the inclusion of muscle-forming cells in the primitive kidney may explain the presence of striped muscle-fibres in a renal tumour. In the kidney also the development of a tumour having the structure of the cortex of the adrenal body has been explained by the discovery of Grawitz that

small islands of adrenal tissue can occasionally be demonstrated within the kidney capsule. Another striking instance of a similar nature is afforded by the small skin-lined cysts or dermoids, which are most common in those situations in which the various parts that unite to form the face come into contact. In such situations it is supposed that a displacement of epiblastic cells into the subjacent mesoblast takes place, and that from these displaced cells the dermoid tumour takes its origin. According to this view, the origin of certain tumours is supposed to be the result of the continued development of cells which have come to lie in the wrong place and are spoken of as "resw of the tumour is, indeed, the result of a malformation. This viets " ; the origin of tumours in cells retaining their embryonic type, and persisting as "rests" among the fully developed tissues, was enunciated and fully discussed by Cohnheim, but the actual demonstrable facts upon which the theory is based are few. It, however, fails to account for the *growth* of the tumour, especially when, as may be the case, the growth occurs comparatively late in life.

Whether or not such a view of the origin of tumours has a general application, it may be accepted as more than probable that a congenital tissue abnormality is a most important element. Some tumours, as, for instance, many angiomas, are themselves present at birth; others undoubtedly originate from cells which are congenitally abnormal, at least in situation; whilst a congenital defect, such as a pigmented mole, may later in life be the starting-point of a malignant growth. The development of a malignant tumour in a congenitally malformed or misplaced part, such as a retained testicle, is another instance of interest in the same connexion. Our conception of the importance of the part played by injury and other accidental agents in the causation of tumours will vary according as we accept or reject the embryonic theory. In the one case an injury can be supposed only to act as the excitant which brings into activity the latent embryonic germs; in the other case we must suppose that traumatism or some other form of external irritant can so influence the normal tissue cells as to modify their mode of growth and determine their development into a tumour. Whichever view be correct, it is impossible to ignore the frequency with which a tumour, especially a malignant growth, such as a sarcoma of bone, follows an injury, for such cases cannot all be explained by supposing that the injury has merely served to draw attention to, or increase the growth of, a tumour already in existence.

Numerous examples could be quoted to illustrate the occasional origin of tumours in connexion with vestigial structures. For instance, certain adenomatous tumours of the uterus can only be explained satisfactorily by the view that they originate in vestiges

of Gartner's duct. Again, the postanal gut or neurenteric canal is generally believed to be the origin of tumours, often of complex structure, occurring in the region of the coccyx, while the vitelline duct and allantois are the source of certain adenomatous tumours of the umbilicus in the adult.

Certain tumours of complex structure (teratomas) illustrate a special mode of congenital origin. There is strong evidence in support of the view that they are closely allied to double monsters, and result from the irregular development of a fecundated ovum within the body of the individual, or from fission of the embryo.

Reference will be made subsequently (p. 493) to the investigations which have been carried out with the object of elucidating the causation of tumours of a malignant nature.

Classification.—The only available grounds upon which a classification of tumours can be founded are: (1) their *structure*, (2) their *origin*, and (3) their *mode of growth*.

For practical purposes it is convenient to adopt the first of these and to classify tumours according to their histological **structure**. This classification possesses the advantage of being based upon actual demonstrable facts and not upon considerations which are more or less theoretical. A classification dependent upon the **origin** of tumours is only possible to a limited degree, and thus fails for practical purpos[illegible]
widely [illegible]
name [illegible]
in the process of tooth-formation. According, however, to a system of nomenclature based solely on structure, an odontoma is a tumour composed of dental tissues, just as an osteoma is a tumour composed of bone. The **mode of growth** of tumours only serves as a basis of classification *in so far as it is the most important feature upon* which the division is made into the *malignant* and the *non-malignant or benign*.

A **benign or simple tumour**, although it may attain enormous proportions, does not, in its most typical form, invade the structures *which surround it*, although in its growth it may, as a result of compression, bring about absorption of the surrounding tissues. Moreover, a common, but not constant feature of a simple tumour is the presence of a capsule, which surrounds the tumour and forms a clear line of demarcation between it and the parts around. A simple tumour only endangers life mechanically, as the result of its size and position. Thus, a small, perfectly simple tumour in the interior of the larynx may prove fatal by causing obstruction to respiration, and a cartilaginous tumour *of the pelvic bones* has been known to cause death by interfering with the act of parturition.

A **malignant tumour**, on the other hand, progressively invades and destroys the tissues of the part in which it grows, and eventually, unless removed, causes the death of the individual. Malignancy is evidenced in two ways: *locally*, by infiltration and the resulting destructive effect of the tumour on the surrounding tissues; and *generally*, by the occurrence of secondary deposits, or metastases, in other parts of the body. This matter will be more fully discussed later, and it is sufficient here to point out that different malignant growths exhibit the local and general evidences of malignancy in very varying degrees. Thus, the tumour of the skin commonly known as rodent ulcer exhibits its malignancy simply by a slowly progressive destruction of the surrounding tissues, without, even in its latest stages, showing any tendency to produce metastases. An example of the opposite extreme is often afforded by certain cutaneous melanotic growths, for, while the primary growth remains as an altogether insignificant pigmented spot, it may already have given rise to widely distributed secondary deposits in the lymphatic glands and elsewhere, which rapidly prove fatal.

It is here necessary to point out that *multiplicity* is in itself no evidence of malignancy. Fatty tumours of the most perfectly benign character may be numbered by thousands, but, although they may differ in age, each tumour is an independent growth, and one is as much primary as another. In the case of multiple malignant growths it can usually be clearly proved that one only is primary, and that the remainder are secondary, not merely in the date of their appearance, but in being actually derived from the primary tumour.

It is thus seen that the distinction between a simple and a malignant tumour depends chiefly upon its mode of growth and its behaviour in relation to the surrounding tissues. The question naturally arises: Can the distinction be made by a histological examination of the tumour itself? The structure of the simple tumour is often described as *typical*, by which is understood that it imitates more or less closely a certain normal type, such as fat, a blood-vessel, or a secreting gland. A malignant tumour, on the contrary, is more or less *atypical* in its structure, and consists of connective-tissue or epithelial cells which take on an irregular and uncontrolled mode of growth, so that although they may retain, in the main, the type of structure from which they have arisen, they show modifications, sometimes to a very marked degree. For instance, a simple glandular tumour of the breast imitates more or less closely the acinous structure of the mammary gland, whilst a malignant growth arising in the glandular epithelium may lose, more or less completely, this feature, and the epithelium may proliferate in a manner entirely unnatural to the gland. On the other hand, the glandular structure may be well preserved, and it may be difficult, in the absence of a clinical history, to differentiate the tumour

from a simple adenoma. In the histological examination of a tumour, with a view to deciding upon its simple or malignant nature, the most valuable information is obtained by observing the appearances presented by the spreading edge of the growth rather than by confining the attention to the details of structure. The microscopic section should, if possible, include not only the tumour, but also the tissues surrounding it, and the pathologist should be very cautious of expressing a final opinion from the examination of a fragment removed from *the centre of the growth.*

The terms "typical" and "atypical," as applied to simple and malignant growths respectively, must be used with some reserve, for, as we have said, the tendency of malignant growths to lose the normal type of the part in which they originate varies greatly. For instance, certain malignant tumours of the thyroid retain in a striking degree the typical structure of the normal gland, and this may be observed not only in the primary tumour, but also in the metastases.

In a classification based upon their structure the following are the tumours which can be recognized as distinct types:—

LIPOMA . .	*A tumour composed of adipose tissue.*
FIBROMA . .	,, ,, fibrous tissue.
MYXOMA . .	,, ,, mucous tissue.
GLIOMA . .	,, ,, neuroglia.
CHONDROMA .	,, ,, cartilage.
OSTEOMA . .	,, ,, bone.
ODONTOMA .	,, ,, dental tissue.
MYELOMA . .	,, ,, red marrow.
ANGIOMA . .	,, ,, blood- or lymph-vessels.
ENDOTHELIOMA .	,, , endothelium.
MYOMA . .	,, ,, muscular tissue.
NEUROMA . .	,, ,, nervous tissue.
ADENOMA . .	,, having the structure of a secreting gland.
PAPILLOMA .	,, having the structure of a papilla.
SARCOMA . .	A malignant non-epithelial growth.
CARCINOMA .	,, epithelial growth
TERATOMA .	A tumour which in its most typical form contains tissue-elements from all the three layers of the blastoderm.

Tumours of mixed structure are very common, and are distinguished by suitable compound names, such as *fibro-myoma*, *myxo-chondroma*, osteo-sarcoma, etc. The fibrous tissue, which in a varying amount is present as the stroma of nearly all tumours, does not indicate a mixed structure unless it is present in such amount as to

impart special characters to the growth. A simple fatty tumour contains a connective-tissue stroma holding together the fat lobules, but it is only when this exists in excessive amount that the tumour is termed a fibro-lipoma.

Clinical examination of a tumour.—Before proceeding to the consideration of the different forms of new growth, it may be useful to indicate some of the most important points requiring observation in the practical examination of a tumour with a view to determining its nature. The **position** of the tumour is often of great diagnostic value, and as far as possible its relation to the neighbouring anatomical structures should be carefully observed. For example, in the case of a tumour in one of the limbs, it is necessary to determine its relation to the surrounding muscles, and whether or not it is connected with the bone. Again, in examining an abdominal tumour, the observer must endeavour to decide whether it is confined to the abdominal wall, or whether it is actually in the abdominal cavity, and in the latter case to search for any evidence of its connexion with one or another of the abdominal viscera Valuable information can often be obtained by noting the effect on the tumour of voluntary contraction of the surrounding muscles, whilst, on the other hand, when the growth is deeply seated, the examination is greatly facilitated by complete muscular relaxation, such as can sometimes only be obtained by the administration of an anæsthetic.

The actual **size** of a tumour is not always at once apparent, for, especially when deeply seated, it is likely to be confused by a want of definition from the overlying tissues.

The **shape** must be accurately noted, and the presence or absence of lobulation of the surface observed

The **consistence** is often a very useful indication in diagnosis, and may vary from a softness suggestive of fluid to a hardness equal to that of bone. When a tumour is soft it may be difficult to decide whether it is solid or fluid, for some soft solid tumours give to the fingers a sense of elasticity, or even fluctuation, which may be very suggestive of fluid. When the observer is in doubt on this point he should carefully examine the edge of the swelling, which, in the case of a soft solid tumour, can often be felt as a distinct, rounded border, whilst if the tumour is fluid no such border is palpable. It is still more important to remember that a hard tumour is not necessarily solid. A tense cyst may be so hard as to deceive the most careful observer. Paget's test is useful in this connexion: A hard, solid tumour is hardest at its thickest part; a hard fluid swelling is least hard at its central, thickest part. Confusion, indeed, arises so often between fluid and solid swellings—as, for instance, between a sarcoma and a chronic abscess—that the surgeon will be wise to adopt every method of

examination for the presence of fluid; and the examination of swellings, which may possibly contain clear fluid, for *translucency* is too often neglected.

In examining the consistence of a tumour, *pulsation is occasionally* observed, and may sometimes be of invaluable assistance, as, for instance, in distinguishing a vascular tumour of a bone from a chronic abscess. Often the pulsation is so slight that it is only detected when the examination is especially directed to it. It can sometimes be elicited, even when not palpable, by *holding the small end of a wooden* stethoscope steadily and firmly on the surface of the tumour and noticing the movements of the opposite end of the instrument. A *bruit* is occasionally audible. The pulsation transmitted to a tumour which lies in the immediate neighbourhood of a large artery must, of course, be carefully distinguished from the true pulsaton of the tumour itself.

The relation of the tumour to the surrounding tissues must carefully be noted, especially as concerns its independent *mobility*. The determination of the fact that a tumour can be moved independently of the tissues surrounding it is often of great importance as a diagnostic sign; the reverse is equally true, and evidence that a growth has become fixed to the surrounding parts may be a physical sign of great moment. Mobility may, however, be misleading, for it may occur *with*, and *not independently of*, the surrounding structures. For instance, a tumour of the neck which has already involved the sterno-mastoid and even the large vessels may, in certain positions of the head, possess a considerable degree of mobility. It is often important to notice whether a movable tumour can be moved equally freely in all directions.

In the case of a superficially situated tumour, it is important to note the *condition of the overlying skin*, especially its colour, the presence of enlarged veins, the presence of œdema, and also to observe whether *the skin can be raised freely from the surface of the tumour* or is more or less adherent to it. When a tumour has actually involved a cutaneous or mucous surface, *ulceration* is common, and a careful examination of the ulcer is likely to prove of valuable assistance in diagnosis. The character of the surface, borders, and base must be accurately noted, as well as that of the discharge. The appearance of the ulcerated surface of a tumour may be so modified by secondary inflammatory changes that its true nature may be obscured; and, again, it must be remembered that the destruction of the tumour substance by ulceration or necrosis may, to a large extent, obscure the evidence that an actual tumour exists. In a doubtful case valuable information may sometimes be obtained by microscopic examination of the discharges from an ulcer, and thus, *for instance, an*

actinomycotic granuloma may be distinguished from an ulcerated tumour. Evidence obtained from the microscopic examination of a fragment removed from the floor of an ulcer may be invaluable, but requires to be considered with much caution.

Finally, it may be pointed out that X-ray examination may prove of great value in the examination of a deeply seated tumour, as for instance in the abdomen or thorax.

BENIGN TUMOURS

LIPOMA

A lipoma may be taken as the most simple example of an innocent growth, because, however long its duration and however large its size, it almost always retains its simple structure unchanged. The most typical lipoma, that met with in the subcutaneous tissue, may conveniently be first described.

Structure.—A lipoma consists of fat, which usually differs slightly in appearance from the normal fat of the part in which it lies. It is often paler in colour, and is composed of larger or smaller lobules which are held together by connective tissue. These give the tumour a very irregular outline (Fig. 35). Surrounding the tumour is a well-marked fibrous capsule, firmly connected with the surrounding tissues, but very loosely connected with the tumour itself. In addition, a very delicate capsule, which forms the surface of the tumour, is continuous with the areolar tissue holding together the lobules of fat. The histological structure of a lipoma is that of normal adipose tissue.



Fig. 35.—Lipoma of subcutaneous tissue, showing marked lobulation.

Clinical features.—A subcutaneous fatty tumour may occur in almost any part of the surface of the body, but the favourite situations are the shoulder and back (Fig. 36). The tumour forms a soft, circumscribed, lobulated swelling; it moves freely on the deep fascia and the overlying skin is usually normal. By careful pressure on the margin of the tumour, its rounded edge can be felt distinctly to slip away from under the finger. Not infrequently the skin over the tumour is slightly dimpled at one or more points, or, if this is

not so, the dimpling can often be produced by grasping the tumour and pressing it up so as to stretch the skin over it. The dimples are caused by the slight traction exerted on the skin by the fibrous bands passing from the cutis to the capsule of the tumour between the lobules. After reaching a certain size, a fatty tumour often remains stationary, and does not necessarily shrink as the result of general wasting. Occasionally such a tumour may, without apparent cause, take on a very rapid growth and reach a large size even in a few weeks.



Fig. 36.—Lipoma of neck. The lobulation of the tumour can be seen.

A fatty tumour is rarely productive of any symptoms, except such as may result from its size or position. Sometimes, however, especially in women, it may be the seat of a varying amount of pain.

In some situations, such as the shoulder and back, a fatty tumour may gradually shift its position under the influence of gravity, and from the same cause the tumour sometimes becomes pedunculated (Fig. 37). A superficial lobule of the tumour occasionally projects through the capsule, and, covered by the thinned skin, forms, as it were, a pedunculated appendage to the main tumour.

The **diagnosis** of a subcutaneous lipoma is rarely attended with difficulty. On account, however, of its very soft consistence, it may be mistaken for a fluid swelling, especially a chronic abscess or a sebaceous cyst. The most characteristic features, which usually serve to distinguish a lipoma, are its distinct lobulation and the presence of a definite rounded border, which slips from under the examining finger. When the edge of an entirely fluid swelling is examined in this way the fluid is displaced, and no definite border is palpable. The distinction between a lipoma and other soft, solid tumours, such as certain soft fibromas and sarcomas, is rarely difficult. In certain

situations a lipoma may simulate some form of tumour peculiar to the part; thus a fatty tumour lying over the breast may be mistaken for a soft adenoma of the gland.

Treatment.—In removing a fatty tumour, it is essential that the capsule be freely opened and the tumour enucleated from it, care being taken that an outlying lobule is not accidentally detached. In prac-

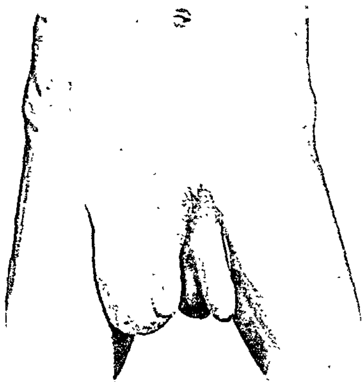


Fig. 37.—Pedunculated lipoma of groin.

tice it is well to carry the incision through the skin and capsule actually into the surface of the tumour, so that the separation of the tumour be not undertaken outside, instead of inside, the capsule.

Modifications of structure.—In the great majority of cases a fatty tumour remains unaltered in structure, however large the size which it may attain, the slight differences in consistence met with in different tumours or in the different lobules of the same tumour being due to a varying admixture of fibrous tissue. As the result of pressure or other irritation, the skin over a subcutaneous lipoma may ulcerate,

and in rare instances this has been followed by suppuration and even sloughing of the tumour substance.

In some cases opaque, whitish areas occur in fatty tumours as the result of necrosis consequent upon a process of saponification, and cavities may form in the tumour, containing a soapy fluid resulting from combination of the fatty acids with the calcium and sodium salts of the plasma. Independently of, or sometimes associated with, saponification, calcification may occur, either in the substance of the tumour or in the form of an eggshell-like layer surrounding one of its lobules.

We know of no recorded case in which it has been certainly proved that a fatty tumour has undergone a sarcomatous metamorphosis A case, however, has been observed by us in which a sarcoma of the skin of the left arm was associated with the presence of multiple fatty tumours of the right forearm and both thighs, and in which the history strongly suggested that such a change had occurred.

Mixed tumours, composed of fat and nævoid tissue (nævo-lipomas), will most conveniently be considered with the angiomas. Certain teratomas also may be largely composed of fat

Multiple subcutaneous lipomas.—These rarely reach a large size, but may be present in almost any number, and may be distributed irregularly over the trunk and limbs, or may be limited in distribution, being present sometimes in symmetrical parts, as, for instance, the two forearms. In some cases the tendency to the growth of multiple lipomas has been hereditary. In Broca's case, quoted by Roger Williams, 2,080 tumours could be counted on the head and neck, trunk, and limbs. The first tumour was noticed on the thigh at the age of 25, and was excised six years later. Subsequently the multiple tumours appeared, and at the age of 70 the patient came under the care of Broca for dysphagia, which eventually caused death. Examination after death revealed the presence of a large fatty growth surrounding the œsophagus and completely occluding it.

It is rarely that any difficulty occurs in the diagnosis of multiple lipomas. From multiple fibromas they can usually be readily distinguished by their lobulation and softer consistence.

Diffuse lipoma.—This variety differs from the encapsuled form in that it forms a fatty mass indistinguishable from the sub cutaneous fat of the part in which it grows. It was first clearly recognized by Sir Benjamin Brodie in 1816. Diffuse lipoma is most common in the neck, especially in the suboccipital regions, where it forms symmetrical tumours over the muscles attached to the occipital bone, and in the anterior region of the neck, forming large

pendulous, lobulated masses, encroaching on the cheeks (Fig. 38). Diffuse lipoma is rarely met with except in fat persons of about middle age, and is much more common in men than in women. Roger Williams, in 1890, was able to collect records of 32 cases of diffuse lipoma. Of these, all except one were in men, and the relation of the disease to chronic alcoholism was brought out in a considerable number of the cases, thus suggesting that these diffuse,



Fig. 38.—Diffuse lipoma of neck.
(*Roger Williams, "Trans. Path Soc," vol. xli*)

fatty growths are closely allied to the large deposits of fat met with in the abdomen and elsewhere in the bodies of drunkards. The condition, indeed, hardly deserves to be included among true tumour-formations, and the name "diffuse pseudo-lipoma" is often applied to it. The constituent fatty tissue presents nothing unusual, but the suboccipital portions of the growth are often unusually firm, and send prolongations among the deep muscles of the part, whilst presenting a more definite border at the level of the superior curved line of the occipital bone.

The operative treatment of these diffuse, fatty growths in the

neck is not very satisfactory, and is rarely called for. Removal of the most disfiguring parts of the growth has, however, been carried out with some success.

While describing diffuse fatty growths in the neck, mention must be made of those occurring in *cretinism* and *myxœdema*. The fatty masses in these cases are present chiefly in the supraclavicular fossæ, and were first described in cretins by Curling in 1850, and in the subjects of myxœdema by Ord in 1878. *Shattock*, who has carefully studied these fatty formations, finds that in the situations in which they occur deposits of a special form of fat can be demonstrated in the human fœtus. The fat cells differ from those of ordinary adipose tissue in the presence of numerous fat globules within a single cell, a peculiarity also met with in certain fatty structures in the neck and elsewhere in some of the lower animals. It has been noticed that these fatty deposits in cretins disappear, like the general excess of fat, under treatment with thyroid.

Diffuse fatty growths in the limbs, sometimes congenital, constitute one form of *macrodactyly* and other varieties of *local gigantism*.

The name "*adiposis dolorosa*" has been applied by Dercum of New York to an unusual condition, met with chiefly in women, and characterized by the association of diffuse and localized fatty formations, especially in the limbs, with severe pain in the affected parts.

Subfascial and intermuscular lipoma.—*Deeply* seated fatty tumours are of practical importance chiefly by reason of the difficulty which often occurs in recognizing their nature. As examples of this variety may be mentioned lipomas occurring beneath the gluteus maximus, in the sole of the foot, beneath the palmar fascia, and in the substance of the tongue. A deeply seated lipoma is especially liable to be mistaken for a chronic abscess. Thus, in a case which came under our notice, the tumour, which lay beneath the trapezius muscle, between the right scapula and the spine, was regarded as an abscess, probably due to tuberculous disease of a rib, until its true nature was revealed by an incision. A fatty tumour in the palm may resemble the swelling caused by tuberculosis of the synovial sheath of the flexor tendons.

Tubby has described a painful form of lipoma of the foot in which the tumour is situated in the inner part of the sole below the internal malleolus. The tumour is diffuse and very vascular.

Parosteal lipoma *is another example of a deeply seated, fatty* tumour, the growth being firmly connected with periosteum. According to Bland-Sutton the tumour is usually congenital, and nearly always contains striated muscle fibres. It has been met with in the bones of the limbs, the skull, the spine, and the pelvis. In a case recorded by

D'Arcy Power, a boy aged 9 years was admitted into St. Bartholomew's Hospital for a soft, painless, elastic swelling on the outer aspect of the upper third of the thigh. The tumour, which before operation was believed to be a chronic abscess, proved to be a large fatty tumour firmly attached by a broad base to the periosteum of the femur below the lesser trochanter. A parosteal lipoma of the calvarium may be distinguished from a sebaceous cyst by its hemispherical shape and fixation to the bone.

Subserous and subsynovial lipoma.—A fatty tumour occasionally arises in the loose tissue external to the serous membranes, such as the pleura and peritoneum. Subperitoneal lipomas have been met with in many different situations, such as the mesentery, omentum, broad ligament, and in connexion with the peritoneum of the parietes. The most important form is that which occupies the retroperitoneal tissue and forms a tumour, sometimes of very large size, behind the abdominal viscera. As a rule, such a tumour originates in the perirenal fat, but Adami, who in 1897 collected 42 cases, found that in some instances the tumour begins in the mesenteric fat, and in others the exact origin is doubtful. As Alban Doran and others have shown, the removal of such a tumour is a very serious proceeding, and in several instances has proved fatal. On the other hand, a lipoma of the omentum may be removed without any serious risk.

Malapert has recorded a case in which a lipoma weighing 6,630 grm. evidently had its origin in one of the appendices epiploicæ of the sigmoid colon. The patient, a woman aged 38, had suffered from a painless enlargement of the abdomen for eighteen months. The tumour was diagnosed as an ovarian cyst, but proved to be a large lipoma attached by a slender pedicle to the sigmoid colon.

Reference may here be made to certain fatty growths not uncommonly met with in the linea alba, especially above the umbilicus, and at the various hernial orifices. Such growths, which may simulate true lipomas on the one hand, or omental hernias on the other, are probably always derived from the subserous tissue, and within the mass of fat a small peritoneal sac is usually present. Fatty tumours of the spermatic cord and labium, although they may occur independently of the presence of a peritoneal sac, probably belong to the same group. In a few recorded cases, as, for instance, one described by McGavin, a tumour of the perineum, closely resembling a perineal hernia, has proved to be composed entirely of fat, the tumour being sometimes associated with an overgrowth of the subperitoneal fat in the lower part of the abdomen.

Closely allied to the subserous lipomas are the fatty growths which are sometimes present over the protrusion of the membranes

in a cranial or spinal meningocele, and it should always be borne in mind that a fatty tumour in the lumbo-sacral region, especially in an infant, may very likely lie over and obscure a small meningocele. It has happened, as the result of this fact, that the operation undertaken for the removal of such a tumour has proved to be far from the simple procedure which was anticipated, and has even resulted in death from meningitis.

The name "arborescent lipoma" has been applied to certain fatty growths occasionally found in joints affected with rheumatoid arthritis. Such formations are in no sense true tumours, but merely represent a modification of the hypertrophy of the synovial fringes so common in this disease. A subsynovial fatty growth may, however, present itself as a localized tumour which, on account of its relation to one of the large joints, is liable to be mistaken for a synovial cyst. Rowlands has recorded a case of this nature, in which a tumour in front of the shoulder, and arising in the subsynovial tissue of the bicipital groove, closely resembled one of the synovial cysts first described by Morrant Baker, and known by his name.

Submucous lipoma.—Fatty tumours may occur in connexion with mucous membranes, as those of the larynx, stomach, intestines, and the conjunctiva. In the intestine a lipoma is an occasional cause of obstruction, and in several recorded cases has resulted in intussusception. Bland-Sutton has recorded the case of a man aged 44 who for seven years had suffered from indefinite intestinal disturbances, which culminated in an attack of threatened obstruction. At the operation a tumour was discovered in the bowel 2 inches below the ileocolic valve, and proved to be a submucous lipoma weighing 2 oz.

Submucous lipomas have been met with in various parts of the larynx, and Shattock has shown that fat cells are present normally in all the positions in which such tumours have been found. In the Museum of the Royal College of Surgeons is a specimen of a lipoma, 1½ inches in its greatest diameter, growing to the left of the middle line beneath the mucous membrane of the adjacent parts of the tongue and epiglottis. The tumour caused sudden death in a man 76 years of age.

FIBROMA

A fibroma is a tumour composed of undifferentiated white fibrous tissue, and varies much in the density of the fibrous stroma and the character and number of the cell elements. In view of the wide distribution of fibrous connective tissue throughout the body, it is remarkable that simple fibrous tumours are by no means common. Although all gradations are met with between the two

varieties, it is usual and convenient to recognize the hard and the soft forms.

A *hard fibroma* tends to assume a more or less globular form, and is often lobulated, although rarely to such an extent as a lipoma. The smooth surface of the tumour is easily separable from the tissues in which it lies, except from the part, such as the periosteum, in which it arises, but no capsule separable from the fibrous substance of the tumour can be defined. When it is cut with a knife a peculiar creaking sensation is felt, and the tough unyielding consistence of the tumour is obvious. The cut surface is usually flat or very slightly convex, and presents a very characteristic appearance, caused by the intersecting glistening bands, like those composing a tendon. Often the fibrous bundles are arranged in closely packed whorls, and the tumour is usually subdivided into lobules held together by looser connective tissue (Fig 39).

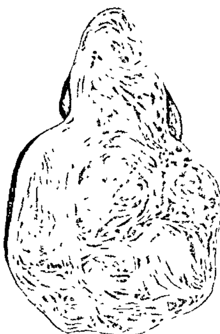


Fig. 39.—Hard fibroma of subcutaneous tissue, showing slight lobulation of tumour and fasciculated appearance of section.

(*University College Hospital Museum*)

Examined microscopically, a hard fibroma presents fasciculi of white fibres which, on account of their irregular intersection, are cut across in different relations to their length. Among the fibres are the small elongated nuclei of the connective-tissue cells (Fig. 40). The blood-vessels vary much in different tumours in size and number. Often they are small and scanty, but in some fibromas large thin-walled vessels are present, which, being unable to collapse by reason of the density of the tissue around them, account for the free hæmorrhage which sometimes occurs when a fibrous tumour is cut into.

A *soft fibroma* differs from the hard variety in its consistence and in the fact that the cut surface of the tumour does not present the glistening appearance caused by the densely packed bundles of white fibres. It consists of loose areolar tissue, the bundles of fibres being slender and forming an open network; the spaces are occupied by serous fluid, which may be present in such

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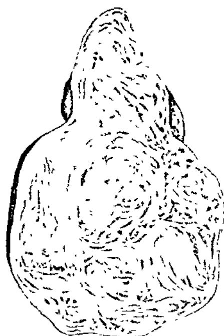


Fig. 39.—Hard fibroma of subcutaneous tissue, showing slight lobulation of tumour and fasciculated appearance of section.

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A *soft fibroma* differs from the hard variety in its consistence and in the fact that the cut surface of the tumour does not present the glistening appearance caused by the densely packed bundles of white fibres. It consists of loose areolar tissue, the bundles of fibres being slender and forming an open network; the spaces are occupied by serous fluid, which may be present in such

amount as to give an œdematous appearance to the tumour, or even produce a close resemblance to a myxoma. Here and there in a fibrous tumour more cellular areas, the cells of which are chiefly spindle-shaped, are often seen, and are probably the situations at which the growth of the tumour is taking place.

Modifications of structure.—Fibrous tumours are liable to mucoid, hyaline, and calcareous degeneration, and when originating in the periosteum not uncommonly show small areas of ossification.

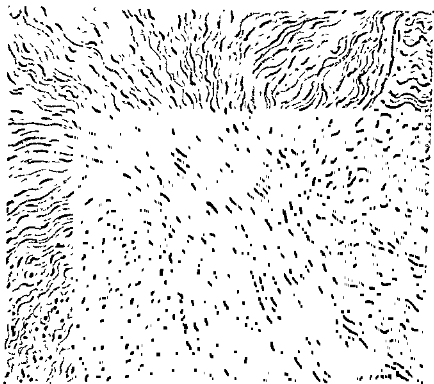


Fig. 40.—Microscopic section of a hard fibroma.

As a result of mucoid degeneration, irregular cavities may form in the tumour, or the whole growth may become transformed into a thick-walled cyst. Tumours of mixed structure in which fibrous tissue forms part of the parenchyma of the growth are not uncommon, as for instance in fibro-myoma, fibro-lipoma, and fibro-adenoma.

Diagnosis.—Many difficulties beset the clinician and the pathologist in the diagnosis of fibrous tumours. From the clinical side it may be pointed out that tumours regarded as fibromas frequently prove on removal not to be so. Inasmuch as fibrous tissue is very widely distributed, fibrous tumours may originate almost anywhere in the body, the position of the growth, therefore, is rarely helpful

in diagnosis. Moreover, the consistence of the tumour varies so much as to be of little assistance. In many tumours fibrous tissue enters so largely into their structure in the form of the stroma that the macroscopic features of the growth are very similar to those of one composed of fibrous tissue only. As examples, it is only necessary to mention such tumours as some forms of fibro-adenoma of the breast and endothelioma of the parotid. Until histologically examined, these tumours may be indistinguishable from a fibroma.

Again, many fibrous overgrowths of a chronic inflammatory nature may closely resemble true fibrous tumours, and indeed the distinction may not be easy even with the microscope. In this connexion it may be pointed out that in a true fibroma the structure is strikingly uniform, whereas in an inflammatory hyperplasia the different stages of the development of the fibrous tissue from the cell elements can be observed, and in some areas the structure may be that of granulation tissue. Moreover, in a fibroma the surrounding tissue elements are displaced without being infiltrated, whereas in an inflammatory fibrous overgrowth the special tissue elements of the part, such as muscle-fibres, are seen to be incorporated in the fibrous growth

Lastly, great difficulty is met with in endeavouring to draw a sharp line between the fibromas and certain varieties of sarcoma. Some of the latter, especially the small spindle-celled forms, may very closely resemble a fibroma, and indeed certain tumours which were formerly spoken of as "recurrent fibroids" are now known to be sarcomatous. Further, a tumour regarded as purely fibrous may recur after removal in a more cellular and obviously sarcomatous form, suggesting that the original tumour was in reality of a like nature.

From these considerations it will be seen that the greatest caution must be exercised before finally deciding that a tumour is a pure fibroma.

Fibrous tumours can arise in almost any part of the body, but the most important sites are the skin and subcutaneous tissue, the fasciæ and muscle sheaths, the nerves, the bones, the submucous tissue of certain viscera, and certain organs, such as the ovary.

Fibroma of the skin may be met with as a hard tumour in the cutis, and occasionally as a circumscribed growth in the subcutaneous tissue. A tumour from the latter situation is illustrated in Fig. 39. When growing in the substance of the true skin a fibroma usually forms a slightly raised hard mass covered by the smooth epidermis, which is intimately adherent to its surface.

A soft fibrous tumour of the skin is not uncommon, and is often known as *molluscum fibrosum*. In many cases the tumours are

multiple, and associated with multiple subcutaneous fibrous nodules. These forms take origin in cutaneous nerves, and will be described later under the heading of Neuro-fibromatosis (p. 400). A single molluscum fibrosum of the skin may, however, occur without any evidence of this mode of origin. *It forms at first a small, soft, conical* projection, which as it increases may become lobulated, pedunculated and pendulous. It has a strikingly soft consistence, and often gives the sensation of an imperfectly filled sac of loose, wrinkled skin.

There is good reason for believing that even the multiple growths having the features of molluscum fibrosum are not always instances of neuro-fibromatosis, but are sometimes simple fibromas. In 1873 John Murray brought before the Royal Medical and Chirurgical Society the cases of three children of one family who were the subjects of multiple growths of this nature, associated with tumours of the gums and mental instability. The growths from one of these patients, who died thirty years later, were investigated by Robinson and Whitfield, and no evidence of nerve-fibres was found in them. The tumours in this case, and in one of the others in which the patient had survived, had greatly increased, so that those on the head gave rise to hideous deformity.

Large, soft, fibrous tumours have often been met with in the ears of the coloured races. They are thought to originate in connexion with the punctures made for the insertion of earrings, and thus to be allied to cheloid.

Cheloid, although not strictly speaking a true tumour, needs passing mention. *It is a fibrous growth originating in cicatrices. A precisely* similar form of cutaneous growth has been met with, especially in the skin over the sternum, in which there is no proof that the growth took origin in a scar. In view, however, of the well-known fact that cheloid may originate in such trivial scars as those resulting from acne, leechbites, etc., it is possible that all cheloids have a similar mode of origin. *A cheloid forms a firm, smooth, whitish or pinkish, slightly raised patch, the margin of which is abrupt and often presents* pointed claw-like processes, from which the name is derived. It is usually tender and is sometimes the seat of spontaneous pain. When originating in an obvious cicatrix the new growth extends from the scar into the surrounding skin, and is thus distinguished from a scar which has merely become hypertrophied. The growth consists of bundles of white fibres which are often almost hyaline in structure. The overgrowth appears to begin around the blood-vessels, and may extend along these beyond the edge of the raised tumour.

Treatment.—A subcutaneous fibroma must be removed by dissection, and cannot be enucleated like a lipoma. In removing a fibrous tumour of the cutis *it is necessary to excise the part of the skin in*

which the tumour grows. The removal of a cheloid by operation is unsatisfactory on account of the tendency of the fibrous growth to recur in the resulting scar, but very satisfactory results are obtained by the use of radium, especially when the treatment is adopted at an early stage.

Fibrous tumours in muscles and fasciæ.—Fibrous tumours are occasionally met with in the fasciæ and in connexion with muscles and their sheaths.

As an example of this variety may be mentioned the fibrous tumours sometimes growing in the abdominal wall, especially in women. Ledderhose found that 90 per cent. occurred in women, and that, of the 90 women, 70 had borne children It thus seems probable that the tumours may in some way be connected with injury to the abdominal wall resulting from stretching. The most common seat of these tumours is the sheath of the rectus muscles, and in their growth they are apt to extend longitudinally in the direction of the muscle-fibres. The diagnosis of a deeply seated fibrous tumour in the abdominal wall may be difficult, but the distinction from an intra-abdominal tumour can usually be made by observing the effect produced on the tumour by contraction of the abdominal muscles. The removal of such a tumour may or may not involve opening the peritoneal cavity; and, if it is of large size, special steps must be taken to strengthen the abdominal wall and prevent the subsequent development of a hernia.

Tumours sometimes occurring in the skin of the abdominal wall are probably closely allied to the more deeply seated fibromas, although in our experience they should be regarded rather as slowly growing fibro-sarcomas—the "recurrent fibroids" of the older surgeons. In the Museum of University College Hospital are two specimens of this nature. In one the strip of skin removed by operation includes a hard fibrous tumour 4·5 cm. in diameter, and several small tumours forming slightly raised smooth elevations on the surface. The patient, a woman aged 52, noticed in her thirtieth year a hard white growth in the skin of the lower part of the abdominal wall after the birth of her second child. Four years later another small tumour appeared near the first and gradually coalesced with it, whilst others formed subsequently. The history of this case suggests a likely origin of the fibrous growths in the lineæ atrophicæ.

Fibroma of nerves.—Much confusion has arisen from the use of the name "neuroma" for a tumour on a nerve, of whatever structure, and from not reserving the name for a tumour composed of newly formed nerve tissue. The confusion is best avoided by naming a tumour of a nerve, as elsewhere, according to its structure.

Fibrous new growths of nerves occur in two distinct forms: (1) as

single or isolated fibrous tumours affecting nerves otherwise normal; and (2) as diffuse fibrous overgrowths included under the general name of diffuse neuro-fibromatosis.

A simple fibroma of a nerve is usually of the hard variety, and may occur on one of the larger nerve-trunks or on one of the terminal ramifications. When situated on a nerve-trunk superficially placed, the connexion of the tumour with the nerve-trunk may be recognized by its position and by the fact that the tumour, although movable in a direction at right angles to that of the nerve, is not movable in the opposite direction. The tumour is usually painless, and, in the majority of cases, unaccompanied by any alteration in the function of the nerve on which it grows. It may project from one surface of the nerve-trunk, or the nerve-fibres may be spread out on the surface of the tumour so as completely to surround it.

When affecting one of the small cutaneous nerves a small fibroma may be exquisitely painful and tender, and for this reason is often spoken of as the *painful subcutaneous tubercle*, a name suggested by W. Wood in 1829. This form of fibroma is more common in women than in men, and is usually met with in one of the extremities, more frequently the lower.

An interesting example of fibroma is that occurring on the auditory nerve. The tumour, arising usually within the internal auditory meatus, which becomes enlarged, occupies the cerebello-pontine angle. *Clinically, it is characterized by progressive deafness* followed by symptoms due to compression of the cerebellum, and later by paralyses of the facial and trigeminal nerves.

The condition to which the name diffuse neuro-fibromatosis is applied is one of extreme interest, and manifests itself in new formations which, in their clinical aspects, present at first very widely different features. The occasional occurrence of multiple fibrous tumours on the cranial, spinal, and sympathetic nerves has long been recognized, and in 1882 von Recklinghausen first pointed out that the soft fibrous tumours of the skin known as molluscum fibrosum were of a similar nature, and recorded two cases in both of which multiple tumours of this nature were associated with multiple tumours on nerves, whilst in one case patches of pigmentation were also present in the skin. The remarkable new growth known as the plexiform neuroma is another manifestation of the same pathological condition, as well as the form of localized hypertrophy of the skin and subcutaneous tissue for which Virchow suggested the name elephantiasis neuromatosa.

The whole subject has been fully dealt with in a monograph by Alexis Thomson, and to this we are indebted for much of the following description. The essential change in neuro-fibromatosis is a diffuse overgrowth of the connective tissue of the nerves, and the diverse

manifestations of the disease can be explained by the extent and limitations of this overgrowth, and the varying changes in the skin and connective tissue which may accompany it. In a normal nerve the fibrous sheath which surrounds it is known as the epineurium; that which surrounds the separate nerve-bundles is the perineurium, whilst the delicate tissue which holds together the individual nerve-fibres of a bundle is called the endoneurium. In neuro-fibromatosis the overgrowth chiefly concerns the endoneurium and the tissue which intervenes between the nerve-fibres and the perineurium. This becomes converted into "a delicate fibrillated network separating the original fibres or lamellæ of the endoneurium; the fibrils of the network are the branching and anastomosing processes of cells; the latter are, for the most part, spindle-shaped with oval nuclei, and they lie either in the spaces of the network, or grasping the endoneurial lamellæ" (Fig. 41). The perineurium is usually unaltered, but the epineurium may be thickened and more compact than usual The nerve-fibres, widely separated, often have a wavy course; there is no evidence of new nerve-formation, and degenerative changes, if they occur at all, are insignificant. The distribution of the fibrous overgrowth varies greatly: in some cases only a single nerve or plexus may be involved; in others the distribution is irregular or even generalized, and thus the spinal and cranial as well as the sympathetic nerves may be affected The change is not limited to the larger nerve-trunks, but frequently extends to the ramifications in the skin and subcutaneous tissue, and even to the intramuscular branches

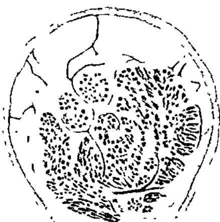


Fig. 41.—Microscopic section of a nerve, showing changes occurring in neuro-fibromatosis. The epineurium is unaltered. There is an overgrowth of connective tissue between and around the nerve fibres.

(*Von Recklinghausen's "Die multiplen Fibroma der Haut"*)

In the formation of *neuro-fibromas* the fibrous overgrowth occurs in excess at one or more spots on the nerve so as to produce localized soft fibrous tumours A tumour of this nature may be solitary and reach a large size, or multiple small tumours, sometimes numbering several hundred, may be present in the subcutaneous tissue of all parts of the body, except the palms and soles. Examination of the nerve shows, however, that the tumour is not the only manifestation

of the disease, for the adjacent parts exhibit cylindrical enlargement, or very frequently the part of the nerve from which the tumour arises is the seat of fusiform swellings due to diffuse overgrowth of the endo-

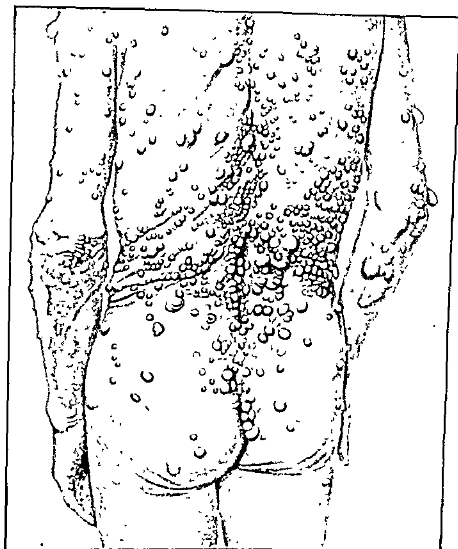


Fig. 42.—Molluscum fibrosum. Multiple cutaneous tumours resulting from neuro-fibromatosis are present. There is a patch of pigmentation on the left forearm.

(J F Payne, "Trans Clin Soc," vol xxii)

neurium. In *molluscum fibrosum* soft fibrous tumours of the skin, usually multiple, are present (Fig. 42). They vary much in size, are often pedunculated, and are covered with thin smooth skin. The tumours consist of soft connective tissue which often extends deeply

beneath the skin from the projecting tumour. It is sometimes possible to feel small convoluted cords in their substance, and the microscope shows that the fibrous overgrowth involves the cutaneous nerve filaments, whilst any other changes present appear to be secondary to this.

Plexiform neuro-fibroma is defined by Alexis Thomson as "a fibromatosis confined to, and at the same time diffused throughout, the distribution of one or more contiguous nerves, or of a plexus of nerves." By dissection it can be shown that the tumour consists of numbers of convoluted cords held together by loose connective tissue. These cords consist of the thickened nerves, which may be cylindrical, fusiform, or beaded (Fig. 43). Plexiform neuro-fibroma is most common in the head and neck in the areas of distribution of the fifth and the superficial cervical nerves, and is much less common on the trunk and limbs, thus agreeing with the form of elephantiasis next to be described. The affection is usually noticed at or soon after birth, but increases subsequently. The tumour, which usually causes no symptom beyond deformity, is often strikingly pendulous, and is covered with skin which may be either normal or pigmented. The most characteristic feature is the peculiar sensation given to the fingers by the convoluted cords formed by the thickened nerves in the tumour. In the scalp the tumour may occupy a groove or an actual opening in the skull.



Fig. 43.—Plexiform neuro-fibroma, dissected to show fibrous thickenings on a nerve. From a case of neuro-fibromatous macroglossia.

(*Spencer and Shattock, "Proc Roy Soc. Med,"* 1907, *vol* i)

In the orbit a plexiform neuroma may occasion some degree of proptosis, and is usually associated with a characteristic swelling in the surrounding parts, such as the temporal region (Fig. 45) In some instances the fibromatosis involves the ciliary nerves, and buphthalmos has been present in many of the recorded cases.

When occurring in the tongue, plexiform neuro-fibroma gives rise to one variety of macroglossia. The first case of this kind was brought before the Pathological Society of London in 1902, by

Shattock and Abbott, and subsequent observations of a similar nature have been made by Thursfield, Billington, Rusca, Delfino, and Spencer and Shattock. In Shattock and Abbott's case the child, 4 years of age, presented an enlargement of the left half of the tongue which had probably been present since birth, although it had subsequently



Fig. 44.—Elephantiasis neuromatosa of neck.
(*Fritsche*, "*Trans. Clin. Soc.*," 1873, *vol.* vi.)

increased. In the submaxillary triangle and upper part of the neck there was a marked fullness which could be felt to consist of knotted cords. Examination of the enlarged part of the tongue after removal showed the nerves to be the seat of a fibromatosis which extended into the conical and fungiform papillæ. The mass removed from the neck was a typical plexiform *neuro-fibroma* which extended into the substance of the submaxillary gland. In Billington's case the tumour of the tongue was associated with multiple subcutaneous

tumours and swellings on various parts of the lumbar and sacral plexuses and their branches; whilst in Spencer and Shattock's case the tumour of the tongue was continuous with a plexiform neuro-fibroma in the neck (Fig. 13), and below the right angle of the mouth was a pigmented molluscum fibrosum.

The condition known as *elephantiasis neuromatosa* (Virchow), and closely allied, as we have said, to the plexiform neuro-fibroma and molluscum fibrosum, is characterized by the fact that the fibromatosis of the cutaneous nerves is accompanied by a diffuse overgrowth of the skin



Fig. 45.—Plexiform neuroma of right orbit and neighbouring temporal region.

(From a case under the care of J H Parsons in University College Hospital)

and subcutaneous tissue of a particular region or segment of the body. When occurring on the head and neck (Fig. 44) the disease presents itself in the form of "large tumour-like masses, often lobulated and complexly folded, sometimes simulating the appearance of the folds of a curtain or of drapery. As they increase in size they tend to hang down and become pendulous or pedunculated" (Alexis Thomson). The overlying skin may be normal, but is often thickened and pigmented. In the substance of the tumour or in the pedicle the thickened convoluted nerves can sometimes be felt, and no sharp line of distinction can be drawn between this condition and the plexiform neuroma.

In the limbs this form of neuro-fibromatosis gives rise to a diffuse enlargement like that present in other forms of elephantiasis, and well illustrated in Fig. 46. The condition is congenital, and the extensive growths usually take their origin in a pigmented spot or a *molluscum fibrosum.*

Reference has already been made to von Recklinghausen's case in which multiple neuro-fibromas, molluscum fibrosum, and pigmentation of the skin were associated. The presence of pigmentation is undoubtedly to be regarded as one of the special manifestations of neuro-fibromatosis, and was present in 19 out of 76 cases collected by Alexis Thomson. It usually takes the form of small brownish spots like freckles, but may involve larger areas, and is most likely to affect the trunk and the proximal parts of the limbs (Figs. 42 and 47).

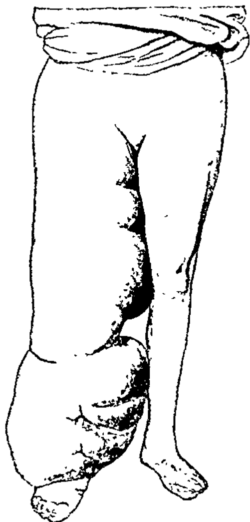


Fig. 46.—Elephantiasis neuromatosa. (*After Alexis Thomson, "On Neuroma and Neuro-Fibromatosis."*)

In a considerable number of cases of neuro-fibromatosis death has resulted from the supervention of sarcoma, to which Garré applied the name "secondary malignant neuroma" (Fig. 47). The malignant change manifests itself clinically by the rapid enlargement of one of the nerve tumours, which may have remained stationary for years. The resulting sarcoma shows a considerable degree of local malignancy, and sarcomatous tumours may also develop on other nerves.

Treatment.—A simple fibroma of a nerve-trunk may sometimes be removed without interrupting the continuity of the nerve. *If removal of part of the nerve is unavoidable, an attempt must be made to repair it* by one of the well-known methods.

A painful subcutaneous tubercle should certainly be removed.

In most of the varieties of general neuro-fibromatosis surgical treatment is not called for. Removal by dissection of plexiform neuro-fibroma and some forms of elephantiasis may be practicable. Elephantiasis neuromatosa affecting a limb has been successfully



Fig. 47.—Sarcoma occurring in a case of neuro-fibromatosis. In addition to a large sarcomatous tumour, a pigmented patch *and multiple neuro-fibromas of skin are seen.*

(*From a case in University College Hospital.*)

treated by amputation. Operation may be urgently called for when the sarcomatous change supervenes in cases of neuro-fibromatosis.

Fibrous tumours of the bones are rare, and there is no doubt that the majority of tumours growing from the periosteum, and to the naked eye presenting the characters of a pure fibroma, prove on both histological and clinical grounds to be fibro-sarcomas, usually of the small spindle-cell form.

Perhaps the most important examples of fibrous tumour of the bones are those of the jaws and the so-called naso-pharyngeal fibrous *polypus*, which is a fibroma growing from the muco-periosteum covering the vault of the pharynx The simplest fibrous tumour of the jaws occurs on the gums, and is known as the *simple* or *fibrous epulis*. The tumour originates in the periosteum of the alveolar border, or in the dental periosteum; it is of slow growth, rarely reaches a large size, and begins as a firm, pale, pinkish tumour arising from the gum, often in the interval between two of the teeth. The tumour must be distinguished from a localized hyperplasia of the gum due to the irritation of a carious tooth or ill-fitting denture, and from the diffuse hypertrophy of the gums which has sometimes been observed in early life. A fibrous epulis has no similarity, except in position, to a squamous carcinoma of the gum, or a myeloma beginning in the interior of the alveolus.

Fibrous tumours of the body of the jaws are also met with. In the upper jaw they may grow from the periosteum of the external aspect of the bone, or from that lining the antrum. In the lower jaw fibrous tumours are occasionally met with in the interior of the bone, and by their continued growth may reach a large size, expanding and thinning the osseous tissue, and finally bursting through it. The accompanying figure shows the right half of a lower jaw, the ramus of which is the seat of a large fibrous tumour of central origin; in parts the tumour is still covered by a thin layer of expanded bone (Fig. 48). The diseased bone was removed by Liston from a man aged 30, in whom the tumour had been observed for two and a half years. In its early stages a central fibroma of the lower jaw can sometimes be easily enucleated after cutting away part of the expanded bone which covers it. In examining a central fibrous tumour, careful search should be made for any evidence of a tooth embedded in its substance, because some fibrous growths of this nature develop from the tooth-sac of an unerupted tooth (the so-called fibrous odontome). Bland-Sutton figures a growth of this kind in a goat, the tooth being embedded in a mass of dense laminated fibrous tissue. In tumours of this nature deposits of calcareous matter may be found.

Fibrous tumours of the naso-pharynx.—These tumours originate from the muco-periosteum covering the under surface of the body of the sphenoid or the basilar portion of the occipital. As it increases, the tumour fills the naso-pharynx and gradually extends into the neighbouring cavities, blocking the nostrils and even extending into the maxillary antra and encroaching upon the orbits. The extraordinary extent to which such a growth may encroach upon the surrounding cavities is seen in a specimen obtained from a child under the care of Richard Quain in 1851. The tumour has extended

along the left Eustachian tube into the tympanum, and, after perforating the membrana tympani, completely fills the external auditory meatus.

Fibrous tumours of the naso-pharynx are most common in young male adults. The earliest symptoms of the disease are nasal obstruction and attacks of epistaxis, which may be profuse and are explained by the vascularity of the tumour. In some instances involution of the growth has been observed, but the usual course is one of steady

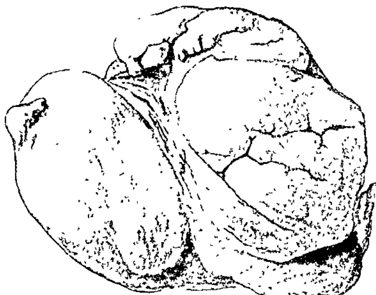


Fig. 48.—Large central fibroma of right half of mandible. The osseous tissue of the body and ramus of the jaw is expanded. The condyle and the incisor portion are unaltered.

(*University College Hospital Museum.*)

increase Extensive operative procedures may be necessary for the removal of such a growth, and, although there may be repeated recurrence from the divided base of the tumour, the evidence appears to us to justify the view that it is a fibroma and not sarcomatous in nature.

Submucous fibromas.—Simple fibrous tumours have been met with beneath the mucosa of the œsophagus, stomach, and intestine. As a rule they are small and not productive of symptoms. In the intestine they may be pedunculated and, like other tumours of the bowel, may give rise to intussusception. W. G Spencer has recorded a case in which he successfully removed a submucous fibroma of the posterior wall of the stomach. The tumour, which is preserved in the Museum

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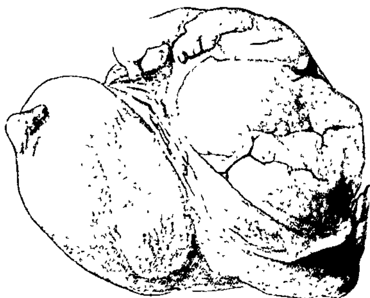


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of the Royal College of Surgeons, has the shape and size of a large kidney, and weighed after removal 7 oz.; it has the structure of a dense fibroma. The patient was a woman, and, as both kidneys were very movable, it was impossible to say to what extent the abdominal pain from which she suffered was attributable to the tumour itself. When the tumour in the stomach was detected at the operation it was at first suspected to be a hair-ball. In recording this case, Spencer refers to a fibrous tumour of the stomach described by Morgagni; it was situated in the posterior wall, weighed about a pound, and was of almost bony hardness

Fibroma of glands and other organs.—Simple fibrous tumours of the various solid organs are extremely rare. In the breast, tumours which to the naked eye appear to be composed only of fibrous tissue prove almost invariably, on histological examination, to be fibro-adenomas. In the Museum of University College Hospital is a remarkable specimen of a pure intracystic fibroma, a large thin-walled cyst being filled with deeply cleft lobulated masses attached by slender pedicles to the cyst wall. Although the lobules of the tumour have an epithelial covering, there is no glandular tissue in its substance. Fibromas of the ovary appear in the early stage as small encapsuled nodules in the substance of the gland. They may, however, reach a size larger than that of a child's head, and, as they increase, the ovarian tissue is stretched over them. In the Museum of University College Hospital are two specimens of fibroma of the penis. In one of these the tumour appears to have originated in the fibrous sheath of the corpora cavernosa immediately behind the glans, and in the other the growth, evidently arising in the region of the corona, has involved the adjacent parts of the glans and body of the penis. Small fibrous tumours sometimes occur in the kidney, especially in the medullary region, but are of no importance surgically.

MYXOMA

A myxoma is a tumour composed of a peculiarly transformed connective tissue, similar to that which is present normally in the Wharton's jelly of the umbilical cord and in the vitreous body of the eye. *In such gelatinous tissue the connective-tissue cells are* branched, and by the union of the processes a delicate reticulum is formed, the meshes of which are occupied by mucus, which stains pink with thionin (Fig. 49) A tumour of this structure has a soft, jelly-like consistence, and in the fresh state ropy mucus can be squeezed from the cut surface. A pure myxoma is undoubtedly very rare, although myxomatous tissue is not an uncommon constituent of tumours of mixed structure. Thus, certain soft fibromas met with in the subcutaneous tissue, and in connexion with nerves, often

present in parts the structure above described. Sarcomas, endotheliomas, chondromas, and lipomas illustrate the same point. Before, therefore, finally deciding that a given tumour is a pure myxoma, it is necessary to submit it to a careful microscopic examination, and certainly not to depend upon the mere fact that the tumour has a more or less jelly-like appearance. Cartilaginous tumours, particu-



Fig. 49.—Microscopic section of a myxoma, showing a reticulum formed by processes of branched connective-tissue cells, the intervening substance consists of mucus. From a tumour of the subcutaneous tissue.

larly in certain situations, are liable to undergo a form of mucous softening of the matrix which gives the growth, in parts at least, a close resemblance to a myxoma.

It is further necessary to remember that certain new formations of inflammatory origin may closely resemble a myxomatous growth. This is especially true of the simple nasal polypus, which was at one time wrongly described as a tumour. Although a nasal polypus consists chiefly of a soft, jelly-like connective tissue, it is undoubtedly the result of a chronic inflammatory hyperplasia of the nasal mucous

membrane, *and all the stages* of its formation can be traced from the earliest stage, in which there is merely a thickening of the mucous membrane in the ethmoidal region of the nasal cavity.

When, however, all *such allied conditions* have been *excluded*, there still remains a tumour which deserves the name myxoma.

It may occur in those situations in which ordinary fibromas and lipomas arise, and clinically is *unlikely to be distinguishable from them.* It has been met with chiefly in the subcutaneous and intermuscular tissue. As an example may be mentioned a tumour of the buttock regarded as a lipoma, which proved on removal to be an encapsuled myxoma extending deeply beneath the gluteal muscles.

Certain soft polypoid outgrowths of the mucous membranes, such as that of the bladder, may have a myxomatous structure.

GLIOMA

A glioma is a tumour composed of tissue resembling neuroglia, the special form of connective tissue found in the central nervous system. Since neuroglia arises from the surface epithelium, a glioma, unlike other connective-tissue tumours, is of epiblastic origin. It occurs only in the brain, spinal cord, and nerves, and in the eye, where it arises in the retina.

Structure.—*Examined microscopically, a glioma consists of* rounded or stellate cells, separated by a felt-work of very delicate filaments, which are believed to be the branching processes of the cells (Fig. 50). In many instances the cells are surrounded by a clear space as in normal neuroglia. The blood-vessels may be abundant, and sometimes present hyaline degeneration. The variations presented by different specimens are dependent chiefly upon differences in the length and number of the fibrils, which may sometimes be so scanty that the cells appear to be in close apposition and the tumour has the appearance of a small round-cell sarcoma.

In addition to this cellular and fibrillary structure, certain peculiar cell-formations—first described by Ströbe in glioma of the brain and by Flexner in glioma of the retina—may be present. They consist of *epithelium-like cells arranged radially around a central lumen*, so as to produce the appearance of a rosette or the section of a tubule. In the case of retinal glioma the cells of these rosette-like formations have been supposed by some pathologists to be rod-and-cone fibres, while those in glioma of the brain have been thought to be derived from the ependymal epithelium.

A *glioma of the central nervous system* may appear as a definite tumour, or may give rise to an enlargement of the affected part, such as the pons, which to a large extent preserves its natural form. A

localized glioma has on section a grey or pinkish-grey colour, varies in consistence, and at its margin passes insensibly into the surrounding brain substance without the presence of a capsule. In the more diffuse form it will be noted that the distinction between cortical and medullary substance is lost. The tumour exhibits no tendency to involve the overlying cerebral membranes. The chief changes occurring in gliomas are cyst-formation, and hæmorrhages, which may be small and scattered, or so extensive as to resemble an apoplectic extravasation. The cystic change may give the tumour a

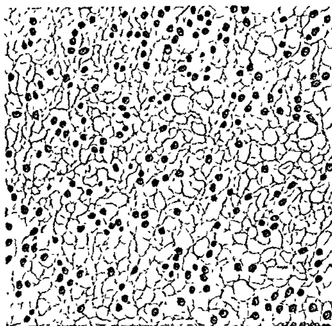


Fig. 50.—Microscopic section of glioma of brain.

honeycomb appearance or may result in the formation of a single cyst, which may be of large size. The glioma usually occurs as a solitary tumour.

A considerable amount of gliomatous tissue is at times present in sarcomas of the brain, just as fibrous tissue may occur in sarcomas generally. Such tumours are called "glio-sarcomas."

Glioma (or neuro-epithelioma) of the retina may be mentioned here, but must be carefully distinguished from ordinary glioma. It is a rare malignant tumour of the retina occurring in young infants. In nearly a quarter of the cases both eyes are affected by growths of independent origin It consists chiefly of small round cells arranged in many layers around fine newly developed blood-vessels; but it

also often contains " rosettes " composed of columnar cells resembling the retinal rods and cones. The whole retina rapidly becomes involved, giving rise to a yellowish reflex from the pupil—the so-called " amaurotic cat's eye." If the eye is not removed, secondary glaucoma supervenes, the growth spreads to the optic nerve and orbital tissues, and metastases are formed in the brain and meninges, in the bones, especially of the skull and face, and in the lymphatic glands. Glioma of the retina is probably derived from a deposit of undifferen-

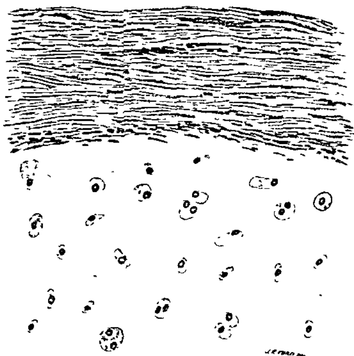


Fig. 51.—Microscopic section of a chondroma, showing cartilage cells lying in a hyaline matrix and fibrous tissue forming the capsule of the tumour.

tiated embryonic retina, which undergoes a delayed proliferation under abnormal conditions, giving rise to a malignant growth. It is thus not strictly a glioma, but resembles glioma in being of neural epiblastic origin.

CHONDROMA

A chondroma is a tumour which has the structure of cartilage, much more commonly of the hyaline than of the fibro-cartilaginous type (Fig. 51). Certain cartilaginous new formations are met with which do not partake of the nature of tumours. For instance, the

irregular outgrowths which occur at the margins of the articular cartilages, especially in connexion with chronic osteo-arthritis, are clearly hyperplastic in nature. Similarly, the cartilaginous outgrowths sometimes occurring in the cartilages of the larynx can hardly be regarded as true chondromas.

In the large joints, especially the knee, cartilaginous bodies occur which originate in the synovial fringes, where cartilage cells can be demonstrated normally. Such bodies often tend to ossify, and, although at first attached by a pedicle to the synovial membrane, frequently become detached and form loose bodies in the joint. These again cannot be regarded as true tumour formations, particularly as they are often associated with, and doubtless result from, chronic joint diseases. Lastly, in the region of the branchial clefts congenital malformations occur in which cartilage may be present. These are best illustrated by the so-called accessory auricles, which consist of a central bar of cartilage covered by skin, and sometimes a muscular layer, and which are seen most commonly in front of the external ear, but sometimes in the neck. A cartilaginous projection of this nature in the neck may correspond with the orifice of a cervical fistula.

Structure.—A chondroma is usually perfectly encapsuled and often very lobulated in outline. Its consistence is firm, but much less hard and resistant than that of bone, and often the tumour gives on examination an almost elastic sensation to the fingers. On section a chondroma is seen to be composed of lobules of cartilage held together by septa of fibrous tissue. The cartilage has a uniform, bluish-grey, almost translucent appearance like ground glass, but is often modified by one or another of the secondary changes in its substance to be described below. As cartilaginous tumours differ considerably in their mode of growth according to the position which they occupy, it will be convenient to describe separately some of the most important varieties.

1. Cartilaginous tumours of the *long bones* occur in two forms, the more common of which is characterized by its tendency to ossification. (*a*) *Ossifying chondromas* are especially common in the long bones of young subjects, and arise very constantly in close proximity to the epiphysial cartilage, being almost invariably attached to the extremity of the diaphysis These tumours, on account of their tendency to ossify, will be considered more fully under the osteomas as cancellous exostoses (p. 421)

(*b*) A much rarer form of chondroma of the long bones occurs, in which the tumour shows no tendency to ossification. It probably originates usually in the epiphysial cartilage, and grows externally, sometimes reaching enormous dimensions. The extreme lobulation of the tumour is an important point in the diagnosis. In one of the

specimens in the Museum of University College Hospital a tumour of *this nature growing centrally in* the lower end of the femur has projected anteriorly and posteriorly through openings in the compact tissue (Fig. 52). In parts the tumour is cystic, and the microscope shows that in some places the softer lobes of the tumour consist of pure *myxomatous tissue*. The patient from whom the tumour was removed was a woman aged 20. A sensation of eggshell-crackling obtained in the tumour led to the belief that it was surrounded by expanded bone, and for this reason the diagnosis of myeloma was made. Nearly four years after amputation was performed the patient was in good health and free from any evidence of recurrence. Cartilaginous tumours of this nature in the long bones must be carefully distinguished from chondrifying sarcomas, which in some instances may consist so largely of cartilage as to resemble very closely a simple chondroma in appearance (p. 519).



Fig. 52.—Chondroma of lower extremity of femur, in section.

2 Cartilaginous tumours are not uncommon *in the hand* in connexion with *the metacarpal bones and* phalanges, and less frequently occur in the corresponding bones of the foot; they are often multiple, and may thus occasion very serious deformity. *A cartilaginous tumour of this nature originates in the interior of the bone*, which is gradually expanded until the growth protrudes through the compact tissue, sometimes forming a mass of considerable size (Fig. 53). In this variety of chondroma the only *modification commonly* met with in the structure of the tumour is calcification (Plate 31). This does not modify the clinical features, but in a section of the tumour is recognized by the presence of small areas of opaque yellow, granular deposit in the semitranslucent cartilage *The calcareous* deposit sometimes occurs also in the strands of fibrous tissue which hold together the cartilaginous lobules.

Ossification is rare, but not unknown, in this variety of chondroma.



Multiple chondromas of the hand. Central tumours are present in the first and second metacarpals, as well as in the first and second phalanges of the index and the second phalanx of the middle finger. The tumour in the second metacarpal is probably extensively calcified.

(From a radiogram by C J Morton)

PLATE 31.

Shattock has described a case of this nature in which, as the result of ulceration of the overlying skin, the ossified part of the tumour underwent necrosis and spontaneous separation; the same writer also refers to a specimen, in St. Thomas's Hospital Museum, of a large

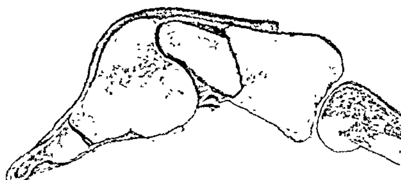


Fig. 53.—Section of a finger, all the bones of which are the seat of central chondromas. The proximal phalanx has been accidentally fractured.

chondroma of the fifth metacarpal bone, the hollowed-out centre of which opens a wide ulcer in the skin. These cartilaginous tumours of the fingers are unconnected with the articular cartilage, and it is indeed interesting to note that there appears to be no recorded



Fig. 54.—Chondroma of a rib, in section. The tumour is attached to the rib close to the costo-chondral junction.

instance of a true cartilaginous tumour originating in articular cartilage.

3 Cartilaginous tumours of large size occasionally grow from the *bony walls of the chest and pelvis*. In the former situation the tumour, whilst projecting externally, may also encroach upon the thoracic cavity. In a case of chondroma of the thoracic wall which *came*

under our notice the tumour projected in the mammary region, and the hard, lobulated growth, pushing the breast forward, simulated to a certain extent a tumour in the breast itself. Although when of large size such a tumour so obscures the ribs as to appear to involve a considerable area of the chest wall, it probably originates from a single rib in the vicinity of the costal cartilage. A small tumour of this nature is illustrated in Fig. 54, the part of the rib, with the tumour attached, having been removed by operation without

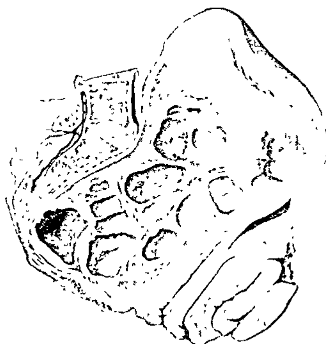


Fig. 55.—Section of a large chondroma of the pelvis. Large cysts resulting from mucoid softening are present in the tumour. The tumour arises from the sacrum, and the rectum, vagina, and bladder are seen between it and the symphysis pubis.

(*This and the four preceding figures are from specimens in University College Hospital Museum.*)

injury to the parietal pleura, which was, however, very intimately adherent to the surface of the tumour.

Similar cartilaginous tumours occasionally arise from the bones of the pelvis. The specimen illustrated in Fig. 55 was from a woman aged 21, who was under the care of Herbert Spencer in University College Hospital. The tumour, which was known to have been growing for seven years, caused obstruction to labour, and death occurred after hysterectomy. Both kidneys and ureters were dilated.

It is an interesting fact that these cartilaginous tumours of the

chest and pelvis appear to show no tendency to ossification, but are liable to mucoid softening with cyst formation (Fig. 55). The tumours illustrate in an extreme degree the lobulation characteristic of chondromas, and the presence of extensive mucoid softening accounts for the fact that some of the most prominent lobules may be elastic, or even give a well-marked sense of fluctuation.

Except in connexion with the bones, cartilaginous tumours are rare. They occasionally grow in *muscles* and *fasciæ*. Erichsen refers to three cases, the tumours being in the tibialis anticus, vastus externus, and pectoral muscles respectively. Liston removed a chondroma as large as an orange from the lower part of the vastus externus muscle of a boy aged 15. It had been growing for three years, and was first noticed two months after a blow. In the Museum of University College Hospital is a small tumour, composed of several lobules of cartilage, which was removed by Marcus Beck from the flexor tendon sheath of the index finger in the palm. Before operation the tumour was mistaken for a ganglion.

Butlin and Spencer refer to congenital cartilaginous and bony tumours occasionally found in the *tongue*, and probably arising in the fœtal structures which give rise to the septum. These authors quote the observations of Nussbaum and Markowski on the septum of the tongue in human fœtuses and new-born children; they describe an encapsuled structure containing fat and sometimes rods or islands of hyaline cartilage, especially near the hyoid bone.

Diagnosis.—The diagnosis of the common varieties of chondroma growing from the bones is rarely attended with difficulty. It is a matter, however, of great practical importance that, in certain malignant tumours, containing cartilage, the latter may so preponderate over the other constituent tissues that to the naked eye the tumour may appear to be a pure chondroma. This will be referred to subsequently in considering chondrifying sarcomas of bone (p. 532). For instance, certain cartilaginous growths affecting the bones of the face must mostly be regarded as of this nature. Christopher Heath, in his "Injuries and Diseases of the Jaws," refers to several striking cases in which a cartilaginous tumour, probably beginning in the maxilla, has gradually encroached upon the neighbouring fossæ, and extended to the orbits and cranial cavity. In Lawson's case ten operations were performed during a period of eighteen years for a recurring cartilaginous tumour of the lower jaw which was undoubtedly a chondrifying sarcoma. A careful histological examination will usually serve to distinguish such a tumour from a pure chondroma. In the latter the lobules of cartilage are held together by a varying amount of simple connective tissue. In a chondrifying sarcoma, on the other hand, the tissue between the

lobules is richly cellular, and generally a gradual transition can be traced between the typical encapsuled cartilage cells lying in a hyaline ground substance and undifferentiated cells with a scanty granular or fibrillated stroma.

The most striking illustration of the fact under consideration is afforded by the historical case of chondroma of the testicle recorded by Paget in 1855. In this case a *tumour of the testicle, composed* apparently of pure cartilage, extended upwards along the spermatic cord and ended in a swelling in front of the vena cava. The growth perforated this vessel and thus reached the lungs, which were the seat of numerous cartilaginous deposits Although doubt as to the purely cartilaginous nature of this tumour had been expressed by Butlin it was not until 1897 that Kanthack and Pigg further investigated the specimen and conclusively proved that the tumour was of mixed structure, which still later investigation has shown to be that of a teratoma (p. 621)

It is probable that in the few recorded instances of cartilaginous tumours of the breast the cartilage has been present in a mixed growth, sarcomatous in nature. It must also be mentioned that, in certain endotheliomas occurring in connexion with the salivary glands and the neighbouring parts, cartilage is a common element in the stroma, and may be so abundant as to give the tumour the clinical and macroscopic characters of a chondroma Finally, cartilage is very often present in teratomas, sometimes in the form of shapeless masses, but in some tumours in a form having a more or less close resemblance to a definite fœtal structure

Treatment.—*A cartilaginous tumour unconnected with* a bone can usually be removed easily by enucleation The cartilaginous tumours of the metacarpal bones and phalanges, when single, may sometimes be removed without sacrificing the finger, or even removing the affected bone. If, however, as is not uncommon, the tumours are multiple, the question of removal must be determined by their size and distribution and the resulting deformity. A chondroma of the chest wall may sometimes *be dealt with by removing the part* of the rib from which it originates.

OSTEOMA

An osteoma or exostosis is a tumour composed of bone.

Bony formations which do not partake of the characters of tumours are very common ; e g. *the osseous deposits which occur on the articular* extremities of the bones in connexion with many chronic joint diseases, and the bony masses sometimes found in muscles as the result of injury. Such chronic inflammatory osseous hyperplasias are of much

practical importance on account of the close resemblance they may sometimes bear to true bony tumours, and will require further consideration from the diagnostic point of view.

Like normal bone, osteoma occurs in two forms, the compact and the cancellous, and develops in a manner corresponding to the two normal processes of ossification in membrane and in cartilage. True osteomas are rare except in connexion with the skeleton.

Cancellous osteoma.—This tumour, which is commonly known as the spongy or pedunculated exostosis, has already been mentioned in speaking of cartilaginous tumours, as the ossifying enchondroma (p. 415). It is essentially an affection of the bones during the period of their growth, and the progressive ossification in cartilage by which the tumour commences and continues its growth is closely correlated with the growth of the bone on which it is situated, for it very rarely continues to increase after the normal period of growth of the affected bone has come to an end, although it often ceases earlier than this. The position in which a spongy osteoma arises from a bone is very constantly the diaphysis in the immediate neighbourhood of an epiphysial line, although as the growth of the bone advances, the distance between the tumour and the epiphysis is proportionately increased (Fig. 56). This very constant position of the tumour gives strong support to the view that it arises in a sequestrated part or "rest" of the epiphysial cartilage, which, being from its isolated position prevented from taking its part in the normal growth of the bone, forms a superfluous bony excrescence or "tumour," but is still more or less subject to the time limits of the growth of the epiphysial cartilage itself. It is also of interest that these tumours are most common at those extremities of the long bones at which the epiphyses continue longest to grow.



Fig. 56.—Cancellous osteoma of upper extremity of tibia, in section.

Examination of a still growing cancellous osteoma shows the following points: The tumour is pedunculated; it may be mushroom-shaped, but more often the bulbous extremity projects obliquely from its constricted base. A fibrous capsule covers the tumour, and

around the attachment of the pedicle is continuous with the periosteum. A layer of hyaline cartilage is present as a cap to the tumour and persists during the period of growth. Around the cancellous bone which forms the centre of the tumour is a thin, compact layer, which, becoming thicker at the pedicle, is continuous with the compact bone of the shaft, while the cancellous tissue of the tumour is continuous through the pedicle with the interior of the bone. Thus, if the tumour is shaved off from the bone, a defect in the compact wall of the latter is exposed, so that septic changes occurring in the wound may readily extend to the interior of the diaphysis—a serious complication which formerly was likely to follow operation. An adventitious bursa is almost always present over the summit of a spongy exostosis, and has been known to be the seat of an inflammatory exudation or extravasation of blood.

Cancellous osteomas are most common at the lower end of the femur, the upper end of the tibia, and the upper end of the humerus. In the first two situations the tumour is more usually situated on the internal aspect of the bone. They are not, however, confined to the long bones, but are met with in the neighbourhood of epiphyses elsewhere, such as the vertebral border of the scapula and the crest of the ilium.

The tumours are more common in boys than in girls, and are sometimes hereditary. They are often multiple. The bones from which they grow are usually otherwise normal, but sometimes impairment of growth or irregular deformity of the bone has been observed, and in some cases of multiple osteomas the bones present evidences of rickets. Gossage and Carling have collected records of 67 families in which more than one member was the subject of multiple cartilaginous exostoses. In these families 199 males and 89 females were affected; in several instances the condition was transmitted through females who were themselves unaffected.

A spongy exostosis is rarely productive of any symptoms other than the presence of the tumour. Pain is exceptional, but some interference with the free use of the part may occur if the tumour is so situated, as in the neighbourhood of the knee, that the adjacent tendons are displaced. In a case under the care of Bilton Pollard a spongy exostosis growing from the ventral surface of the scapula near the vertebral border in a young girl so raised the bone from the chest wall as to suggest at first sight the deformity so commonly met with in latero-rotatory curvature of the spine. An exostosis of the pelvis has been known to cause insuperable obstruction to normal delivery.

The *subungual exostosis* deserves special mention. It is most common on the dorsal surface of the distal phalanx of the great toe,

and is said to be most frequently met with in females. It causes intense pain as it projects upwards beneath the edge of the nail. The latter becomes brittle and breaks away, exposing the tumour, still covered by the nail matrix. Ulceration is then likely to occur, and the growth of exuberant granulations obscures the small bony tumour beneath. *The structure of the tumour is identical with that of other cancellous exostoses.* It is very rare except on the great toe, but has been seen on the fingers, where, in one case, the pain caused by piano-playing first drew attention to the presence of the tumour.

The removal of a spongy exostosis presents no special difficulties, but it is *essential that no part* of the cartilaginous covering be left. The subungual exostosis can be removed after avulsion of the nail, and amputation of the toe is very rarely necessary.

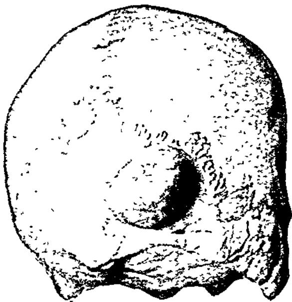


Fig. 57.—Compact osteoma of tabular portion of occipital bone.

(*University College Hospital Museum.*)

Compact osteoma.—This variety of bony tumour, which, on account of its extreme density, is known as the "ivory exostosis," usually occurs in situations which indicate its origin independently of cartilage. It is generally attached to the surface of a bone and, unlike the *spongy exostosis, is sessile.*

An ivory exostosis is most common on the vault of the skull, especially the parietal and frontal bones, where it forms a slowly growing, and usually small, sessile tumour of extreme hardness, over which the scalp moves freely. The tumour is usually single, but not very rarely two or more may be present. When quite small it is usually hemispherical, but as it increases it tends to become conical or limpet-shaped (Fig. 57). Extremely dense osteomas have occasionally been met with on the inner aspect of the skull, and have necessitated operative interference on account of symptoms caused by pressure on the brain. As a rule, tumours in this situation are more

irregular in shape and less smooth on the surface than those of the external aspect of the skull.

Ivory exostoses occasionally grow in the frontal and sphenoidal sinuses and ethmoidal cells, the tumour probably originating in the periosteum lining the cavity. When such a tumour occupies the frontal sinus the first symptoms are those of a slowly increasing distension of the sinus, but later the tumour may project into the orbit, displacing the eye outwards, downwards, and slightly forwards. Specimens are in existence of enormous tumours of this nature, resembling large nodular masses of marble, and encroaching on the cranial cavity (Fig. 58). Ivory exostoses may not only extend into the orbit from the frontal sinus, but occasionally originate in the orbit, usually from the upper border.

Bony tumours, sometimes reaching a large size, and of dense or cancellous structure, occasionally occur in the jaws. In the maxilla the tumour may originate on the external aspect of the bone or in the antrum ; in the mandible it may be central or periosteal. Ivory-like osteomas of the mandible are most likely to occur in the region of the angle.

Another unusual site for an osteoma is the external auditory meatus, where the growth may be either ivory-like or cancellous. Loss of hearing and other results may follow the blockage of the meatus.

It is doubtful if a true osteoma ever occurs except in connexion with the skeleton, and probably small tumours of the skin and other parts which have been described as bony would prove on investigation to be merely calcareous. Small osseous deposits occur in other growths, such as chondroma and fibroma, while the ossifying sarcomas will be considered subsequently (p 520). Bone is a very common constituent of teratomas, in which it may take the form of fœtal parts

Diagnosis of osteomas.—The recognition of the common forms of osteoma is usually easy. In pedunculated osteoma of a long bone, confusion has been known to arise as the result of effusion into the overlying bursa. A small bony prominence in the neck above the clavicle is probably a cervical rib, and must not be mistaken for an exostosis. An ivory exostosis on one of the cranial bones can hardly be mistaken for a periosteal node.

Extensive ossification of a sarcoma may occasionally lead to a mistaken diagnosis, and indeed such a tumour may appear on section to be a simple osseous growth.

Certain inflammatory bone-formations may closely resemble osseous tumours, although in these circumstances the more diffuse character of the enlargement is likely to resemble an ossifying sarcoma rather than a simple osteoma.

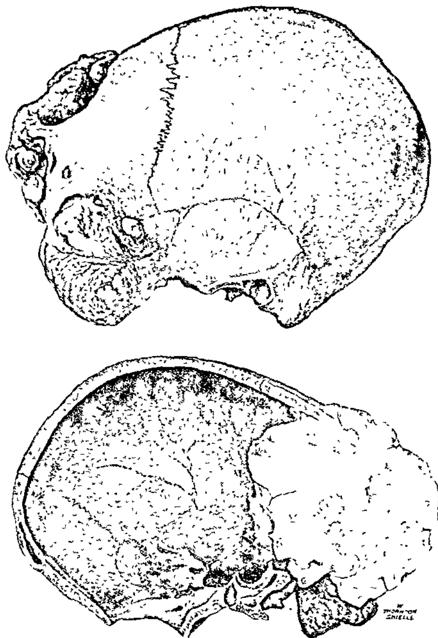


Fig. 58.—Large ivory exostosis, probably originating in one of the frontal sinuses. The tumour has expanded the bone and encroached upon the cranial cavity, orbits, and neighbouring parts.

Pathological Museum of the University of Cambridge.)

In this connexion the extraordinary deposit of new bone which may gradually occur around a small sequestrum is of great practical importance. To this condition Paget applied the graphic name of "quiet necrosis," and every surgeon should *remember the case* in which amputation was performed at the hip-joint for a supposed ossifying tumour of the femur, but in which the enlargement of the bone was due to chronic osteitis around a central sequestrum. In the lower jaw instances of the mimicry of an osseous tumour by chronic inflammation of the bone are not uncommon. A specimen in the Museum of University College Hospital well illustrates this point. It consists of part of the right side of the body of the mandible removed by operation for a supposed bony tumour. In the interior of the dense mass of bone is an irregular cavity containing an imperfectly *separated sequestrum and the fang of a tooth.*

In connexion with bony tumours of the jaws, it may be remarked that some of those recorded as central osteomas have been examples of odontoma; and reference must also be made to the rare disease to which Virchow gave the name *leontiasis ossium.* This affection usually begins in early life as a thickening of one of the facial bones. Very gradually the enlargement extends and may spread eventually to all the facial bones and those of the cranium, producing diffuse enlargements and hyperostoses which encroach upon all the neighbouring cavities, producing hideous deformity and various symptoms *due to obstruction to respiration and pressure on the brain and cranial* nerves. The affected bones are converted into thick masses of spongy, osseous tissue, the spaces of which are occupied by fibrillated tissue. Nothing is known concerning the cause and nature of the disease, and it is only in the earlier stages, when it is limited in extent, that it can at all resemble an osseous tumour. In some cases of endothelioma of the dura mater the growth invades the overlying skull and leads to the formation of a *localized thickening of the* bone, which may cause a hemispherical swelling on the external surface. Such a condition may be mistaken for a primary bone tumour.

Treatment.—An ivory exostosis of the outer surface of a cranial bone rarely requires removal. Bony tumours of the frontal sinus have occasionally been removed by opening the enlarged cavity and separating the tumour from its site of attachment. In the auditory meatus the removal of an osteoma may be an urgently necessary but difficult procedure. Speaking generally, it may be said that *when practicable an* ivory osteoma should be removed by dividing the bone from which it arises rather than by the older and more difficult method of gradually dividing the base of the tumour itself.

ODONTOMA

In a classification of tumours based entirely upon structure the name "odontoma" must be restricted to those bonelike tumours which consist of one or more of the special dental tissues—enamel, dentine, and cement. At the present time, however, it is customary, following Bland-Sutton and other pathologists, to employ the term in a much wider sense, and to define an odontoma as "a tumour composed of dental tissues in varying proportions and different degrees of development, arising from teeth-germs, or teeth still in the process of growth." It will be seen that, according to this definition of odontoma, all tumours which are believed to owe their origin to errors and irregularities in the development of the teeth, however widely they may differ in structure, are included under this name

The chief facts concerning the development of the teeth may briefly be mentioned. From the epithelium of the gum a downgrowth (dental epithelium) occurs into the mesoblast and, becoming thickened at the sites of the future teeth, forms the special enamel organ from which the enamel is developed. Into the deep surface of each enamel organ a process of the mesoblast projects—the dental papilla—and from this the dentine and the pulp arise. Around the enamel organ and papilla a layer of condensed vascular mesoblast forms the dental sac, from the inner part of which the layer of cement which covers the dentine of the fang develops. The dental sac and its contents are together known as the tooth-follicle.

The development of those permanent teeth which replace the temporary set is in all essential respects similar, except that the enamel organ, instead of being formed by a direct downgrowth from the surface epithelium, arises as a bud-like thickening on the strand of epithelium (tooth band) which connects the enamel organ of each temporary tooth with the surface.

From this it is evident that tumours of very varying structure—epiblastic and mesoblastic—can arise in connexion with the changes concerned in the development of the teeth, and, as Broca has shown, the actual structure of the tumour will depend upon the period at which it arises.

In 1885, Malassez published some important observations in which he was able to show that epithelial cells, representing parts of the common enamel-germ which are not actually concerned in the formation of the enamel organ, may still remain in the adult jaw. To these epithelial remains he gave the name "débris épithéliaux paradentaires," and it is probable that certain cystic and epithelial tumours of the jaws originate in them.

Following the classification adopted by the Committee of the

British Dental Association, which is a slight modification of that originally made by Bland-Sutton, the following varieties of odontoma are recognized :—

1. **Epithelial odontome.**—The three varieties of odontome included under this heading and characterized by their origin in the *dental epithelium* are the *multilocular* cystic tumour, dentigerous cyst, and dental cyst.

(*a*) **Multilocular cyst.**—Occurring much more commonly in the mandible than in the maxilla, this tumour presents itself as a central growth which gradually expands a considerable part of the body and often the ramus of the jaw into a thin, irregular bony shell. The tumour itself, as the name implies, is composed of a number of cysts mixed with a variable amount of *solid tissue*. *Sometimes* the solid growth forms the bulk of the tumour, which has then the macroscopic characters of a fibroma in which the cysts may be scarcely visible, whilst in other cases one or more of the cysts attain a considerable size, or the cysts are uniformly *small* and the whole tumour has a honeycomb appearance. The expanded bone of the mandible, especially of the outer table, is often so thinned as to give the well-known sensation of eggshell-crackling The teeth in the affected part of the jaw become loosened, and in the place of those which have come away the tumour projects beneath the gums, and one or more sinuses may lead into cysts in the growth

Examined microscopically, the solid parts of the tumour present a connective-tissue stroma in which are branching spaces, filled with epithelial cells The cells forming the peripheral layer of the cell-masses are usually cubical or columnar in shape, while the remaining *cells are small, and elongated or angular. The formation of cysts is* due to changes in the masses of epithelium, the central cells of which undergo degeneration, while the peripheral cells remain as a lining to the cyst (Fig 59)

The tumour usually occurs in young adult women, and pursues a slowly progressive course often extending to many years.

The epithelium of the tumour probably arises from some part of the downgrowth of the epithelium which is concerned with the development of the teeth, or in the remains of this epithelium described by Malassez. It is probable that in some cases a tumour of this nature may arise directly from the deeper layers of the epithelium of the gum. The resemblance of the histological structure to that of basal-cell tumours of the skin is indeed very striking.

(*b*) **Dentigerous cyst.**—This variety of epithelial odontome (also known as follicular odontome) occurs as a single cyst, found rather *more commonly in the mandible* than in the maxilla. The cyst is lined by an epithelial layer of varying thickness, which has

been known to assume a papillary arrangement, and in rare instances has presented in parts a structure similar to that found in multilocular cysts. It usually occurs in connexion with a tooth of the permanent set, most commonly a canine, but rarely the tooth in the cyst is supernumerary, or one of the temporary set. The tooth itself is often incompletely developed, and its crown projects into the cavity



Fig. 59.—Microscopic section of cystic epithelial tumour of mandible.

of the cyst The cyst as it increases causes expansion of the mandible, and when occurring in the maxilla may extend into the antrum, and eventually the bony shell may become so thin as to yield on pressure with the finger and give the sensation of eggshell-crackling. Secondary changes due to inflammation may occur. The diagnosis of a dentigerous cyst from other central tumours is usually suggested by the absence of one of the teeth in the position of the enlargement, and may be rendered certain by radiography.

(c) Dental cyst.—This form of epithelial odontome occurs a cyst in connexion with the permanent and normally erupted to It is usually single, and occurs at any age and in either jaw. cyst may reach a considerable size, expanding the bone and extend into the antrum. Suppuration with the formation of sinuses oper into the mouth is not uncommon. An epithelial lining can gener be demonstrated in the cyst. This is supposed to arise from the mains of dental epithelium, but the fact that cysts of this vari usually arise in connexion with infec teeth suggests that they are inflammat in nature.



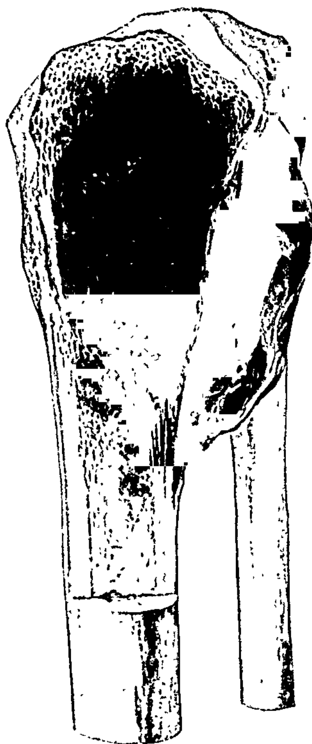
Fig. 60.—Composite odontoma, in section. The tumour consists of a marble-like mass of dental tissues.

The treatment of multilocular c consists, when possible, in the removal the tumour, but in some cases resection some part of the jaw may be unavoidal Dentigerous and dental cysts should be fre opened from the mouth, any unerupted to in the former extracted, the lining remove and the size of the cavity reduced as mu as possible by crushing together the panded layers of the bone.

2. **Composite odontome.** — Co posite odontomes are "dependent up aberration of the enamel organ with oth dental tissues." Numerous varieties a recognized, which need not be describ here.

The "complex composite odontome represented in Fig 60 was removed Christopher Heath from a young woma of 18. The tumour had caused expansio of the right half of the lower jaw with suppuration. A patch apparently bare bone could be felt within the mouth, and it was at fir doubtful whether the case was one of simple necrosis or of necros secondary to the growth of a tumour in the bone. Eventually th tumour was removed with an elevator without sacrificing any part the jaw. This case illustrates the difficulty which may occur in th clinical diagnosis of an odontome, and the importance of distinguishin it from a tumour of the bone so that an unnecessarily sever operation may be avoided.

3. **Connective-tissue odontome.**—Under this heading are included fibrous odontomes and cementomes. A fibrou odontome results from fibrous thickening of the dental sac and presents itself as a central fibrous tumour of the jaw in which an un-



Myeloma of upper extremity of tibia.

(From a specimen in the Pathological Museum of the University of Cambridge.)

PLATE 32

erupted and often imperfectly developed tooth is embedded. These tumours, whether occurring in man or in the lower animals, are believed to result from rickets. A cementome occurs as an irregular osseous tumour connected with the fang of a tooth. Cementomes have been known to reach a large size, and must be distinguished from osteophytic outgrowths.

MYELOMA

A myeloma is a tumour which in its structure corresponds more or less closely to that of red bone-marrow.

Structure.—Examined microscopically, the most striking feature of the tumour is the presence of numerous large multinucleated cells

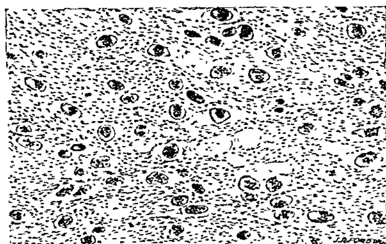


Fig. 61.—Microscopic section of a myeloma.

—myeloplaxes (Fig. 61). These cells are usually rounded or oval in shape, with a regular outline, and the nuclei, often twelve or more in number, are arranged centrally or irregularly throughout the cytoplasm. The stroma varies in different specimens, consisting usually of small oval cells in a finely fibrillated matrix, but occasionally containing a considerable portion of fibrous tissue. The blood-vessels are very numerous. A myeloma on section presents a homogeneous appearance and has a characteristic dark-red or maroon colour (Plate 32). It has a peculiar consistence, and its friability has been compared with that of the liver. The colour of the tumour is often modified by extravasations of blood into its substance, so that mixed with the dark-red tissue may be seen areas of a dark chocolate-brown tint. As a further result of extravasation, degenerative changes are common

in the tumour, and cysts frequently form, sometimes so extensively as to obscure the true nature of the growth.

It was formerly customary to include the myelomas among the sarcomas as the giant-cell variety, or myeloid sarcoma. The course of the disease, however, fully justifies the view that a myeloma is a

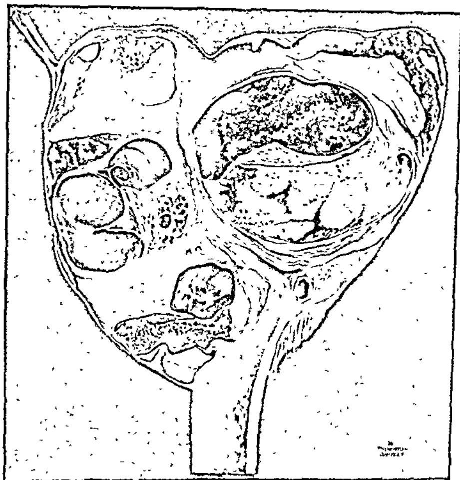


Fig. 62.—*Myeloma of tibia, in section. The tumour has expanded the upper extremity of the bone and undergone extensive cystic changes.*

(*University College Hospital Museum.*)

benign growth, showing no tendency to cause deposits in the lymphatic glands or other metastases. It is undoubtedly true that in many forms of rapidly growing sarcoma multinucleated giant cells are present, but this feature *alone does not justify the inclusion of such tumours* with the myelomas. The true myeloma presents macroscopic and histological characters which are *quite characteristic*, and it may

safely be concluded that giant-cell tumours exhibiting evidences of malignancy are sarcomas and not myelomas.

Clinical features.—Myelomas are met with almost exclusively in the bones, and are much more common in the long bones than elsewhere, beginning usually in the interior of the shaft, close to the epiphysis. As the tumour grows it gradually expands the bone and extends into the epiphysis, often up to the articular cartilage, which, however, even in the later stages of the disease when great enlargement of the articular extremity has resulted, almost invariably remains intact, and prevents the tumour from reaching the joint cavity (Fig. 62). As the bone expands it usually becomes progressively thinned, and at a certain stage the bony layer surrounding the tumour may at parts give the eggshell-crackling sensation under the pressure of the finger. At a still later stage the bony shell becomes *entirely absorbed at one or more spots, and the tumour projects* from the interior of the bone, and can be felt as a softer lobe on the surface of the otherwise bony enlargement. On account of the great vascularity of the tumour, pulsation can often be detected at any spot at which the bony envelope of the growth is wanting, and is a physical sign of great value in the differential diagnosis.

As already mentioned, the substance of a myeloma may be very extensively broken down by hæmorrhage In some cases this occurs to such an extent that the whole tumour is transformed into a mere blood-cyst of the bone, the true nature of which can only be demonstrated by microscopic examination of the thin layer of soft tissue which usually lines the cavity in the bone. In the case from which Fig 63 was drawn, the superficial part of the cyst which projected from the posterior surface of the upper extremity of the tibia formed an elastic swelling in the popliteal space.

Myeloma is most common in the lower limb, especially in the upper extremity of the tibia, it is not uncommon in the lower extremity of the femur, and has also been met with in the fibula, especially the upper end, and in the patella. In the upper limb the most common site is the upper extremity of the humerus; in the forearm bones the lower extremities are more often affected than the upper; in the clavicle, myeloma of the sternal end is less rare than of the acromial end.

In a case recorded by Haussling and Martland of Newark, N J., multiple tumours having the characteristic histological structure of myeloma were present and involved several of the long bones, both clavicles, maxilla, rib, and pelvis.

Diagnosis.—The difficulties which may be encountered in the early recognition of a myeloma of the extremity of a long bone are chiefly concerned with its distinction from other conditions causing

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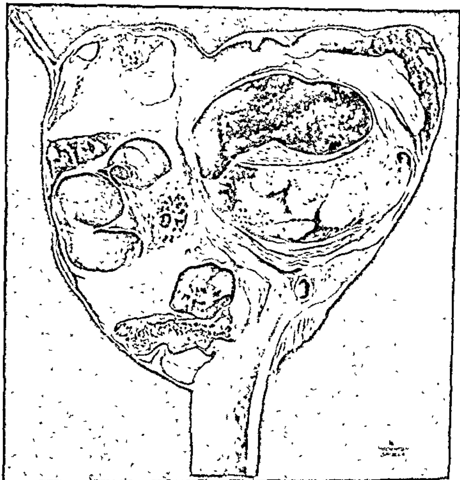


Fig. 62.—Myeloma of tibia, in section. The tumour has expanded the upper extremity of the bone and undergone extensive cystic changes.

(University College Hospital Museum.)

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Diagnosis.—The difficulties which may be encountered in the early recognition of a myeloma of the extremity of a long bone are chiefly concerned with its distinction from other conditions causing

enlargement of the bone and from certain affections of the neighbouring joint In the early stages a myeloma may closely resemble certain chronic inflammatory enlargements of the bone, such as may result from tuberculous disease, chronic staphylococcal abscess (Brodie's



Fig. 63.—Myeloma of upper extremity of tibia, in section.
(University College Hospital Museum)

abscess), and syphilitic osteitis. Certain cystic formations may also closely resemble a myeloma. It has already been stated that occasionally a myeloma itself becomes transformed into a cyst, but, apart from this, single or multiple cysts, the pathology of which is not yet clearly determined, occur chiefly in the long bones. In some

instances the cyst probably arises as a result of the disease of bone first described by von Recklinghausen and known as "osteitis fibrosa." Such a cyst, if occurring singly, as, for instance, in the upper part of the humerus of a young subject, may very closely resemble a myeloma The differentiation between a myeloma and a central sarcoma can hardly be made by the clinical features, but in some cases both these tumours may present a soft pulsating area on the enlarged bone which will with certainty distinguish them from inflammatory forms of enlargement. In a doubtful case X-ray examination will prove of great value. (Fig. 64) It must, however, be admitted that in some instances, after the most careful consideration of the history and all other aspects of the case, the nature of the bony enlargement still remains uncertain, and can only be elucidated by a thorough exploration of the interior of the bone.



Fig. 64.—Radiogram of a myeloma in the lower extremity of the radius.

(*Eve, "Clin Soc. Trans," vol. xxxiii.*)

In the later stages a myeloma of the articular extremity of a long bone may closely imitate articular disease, although by careful examination such a mistake is usually avoidable. In the case of myeloma of the tibia from which Fig 62 was taken, the patient, a woman aged 42, had been treated for three years for chronic rheumatism of the knee-joint; but the mistake which has most often been made is to confound a myeloma of the femur or tibia with tuberculous disease of the joint.

It must be remembered, further, that a pulsating tumour of a bone, such as a myeloma or sarcoma, may present a superficial resemblance to an aneurysm, as, for instance, when the pulsating part of the tumour projects from the femur or tibia into the popliteal space, or from the humerus into the axilla.

Myeloma of the jaws is more common in the mandible than in

more rapid growth, softer consistence, and darker colour. Occasionally, however, a tumour having the clinical features of a fibrous epulis is found to contain giant cells and is really a myeloma, so that in removing a fibrous tumour of the gum it is wise to remove the superficial part of the bone beneath the tumour. In other cases the tumour, when affecting the mandible, extends into the body of the bone, expanding it and thinning the osseous tissue so as to allow eggshell-crackling to be demonstrated. In the maxilla the tumour may in rare instances extend into the antrum. The expansion of the mandible caused by a central myeloma must be distinguished from various inflammatory enlargements and from other central new growths, especially a dentigerous cyst

Treatment.—The least extensive measure which can be applied to the removal of a myeloma is to open up the affected part of the bone and thoroughly clear out the tumour together with the surrounding osseous tissue. Such a simple measure has been successfully adopted in certain myelomas of the jaws and even of the long bones of the limbs. In some situations, as, for instance, when the disease involves the upper extremity of the humerus, the head of the fibula, the head of the radius, the lower ends of the radius or ulna, or either end of the clavicle, a good result has followed excision of the affected part of the bone. In a case of myeloma of the patella, Lister removed the bone and excised the articular extremities of the femur and tibia in order to secure ankylosis of the knee. When amputation is inevitable, as is usually the case in myeloma of the lower end of the femur or the upper end of the tibia, the limb may safely be removed immediately above the disease.

Myeloma of tendon sheaths.—Numerous cases are on record in which an encapsuled tumour situated within a tendon sheath, most commonly in one of the fingers, has proved by microscopic examination to have the structure of a myeloma. In several of the cases there has been a history of injury The tumour illustrated in Fig 65 was removed by Billington, of Birmingham, from the ring finger of a boy aged 14. It had been noticed for a year, and was supposed to have resulted from the blow of a cricket-ball. The tumour, which was about the size of a kidney-bean, lay in the flexor tendon sheath over the middle phalanx. The palmar surface of the phalanx was shown by X-ray examination to be eroded as if from pressure, but the tumour was unconnected with it.

Diffuse myelomatosis.—Before leaving this subject it may be well to point out that the name *myeloma* or *myelomatosis* has been applied to diffuse tumour-like formations of the bone-marrow occurring in certain rare cases, and in several recorded instances associated with the presence in the urine of the peculiar protein

substance first described by Bence-Jones. The disease is also known by the names of *myelopathic albumosuria* and *Kahler's disease*, and has been studied in this country especially by Bradshaw and Parkes Weber, in whose writings a full description of the recorded cases will be found. The diffuse deposits, which differ essentially from myeloma in their histological characters, affect chiefly the vertebræ, sternum,

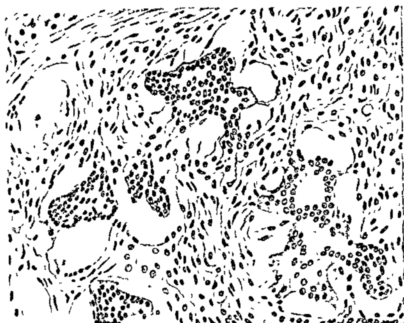


Fig. 65.—Microscopic section of myeloma of tendon sheath.

and ribs, less commonly the bones of the limbs, and may cause localized outgrowths on the bones. The softening of the bones due to the absorption of the osseous tissue may be followed by gradual alteration in shape, producing in the case of the spine marked kyphosis

ANGIOMA

An angioma is a tumour of vascular structure, a *hæmangioma* being composed of blood-vessels, and a *lymphangioma* of lymphatic vessels Tumours of this nature are most commonly congenital, and are frequently known as vascular nævi, those composed of lymphatic vessels being distinguished as lymphatic nævi. The word nævus strictly means a mole or natural mark, and is frequently employed to include pigmentary and other congenital marks on

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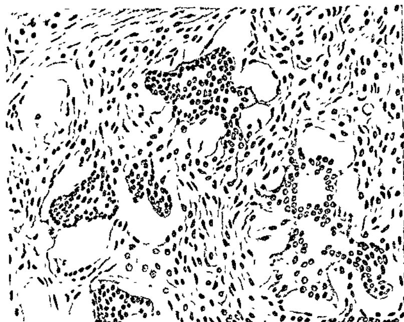


Fig. 65.—Microscopic section of myeloma of tendon sheath.

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the skin ; but in the more common use of the term it is understood to mean a hæmangioma, whether congenital or acquired.

HÆMANGIOMA

Tumours composed of blood-vessels are divided, according to the character of the constituent vessels, into capillary, arterial, venous, and cavernous, of which the capillary and cavernous are the most common. Some confusion has arisen from the use of the terms venous and cavernous in this connexion as if synonymous. A cavernous nævus, however, does not consist of vessels resembling veins, but

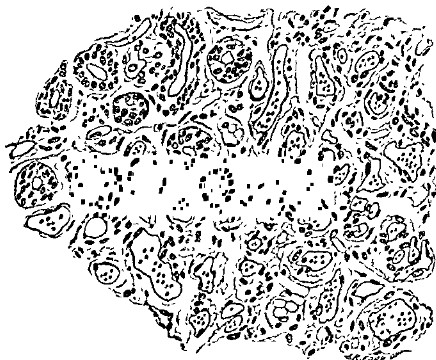


Fig. 66.—Microscopic section of a capillary angioma, showing capillary blood-vessels, the swollen endothelium of which gives them in some parts a gland-like appearance.

imitates the structure of the cavernous or erectile tissue met with in the penis and elsewhere.

Capillary angioma.—If a capillary nævus is examined microscopically, it is found to consist of closely packed capillary vessels which, on account of their irregular arrangement, ar divided in various directions. The endothelial cells are often arranged in several layers, and thus the lumen may be very small, and the close approximation of the vessels may give a very cellular appearance to the section (Fig. 66). *In other cases the capillary vessels are separated by more*

abundant connective tissue, often containing fat cells, and in the skin the capillary network passes irregularly among the sweat- and sebaceous glands and hair-follicles. The capillaries not infrequently present small saccular dilatations.

Capillary angiomas are most common in the skin, and are popularly known as "mother's marks," or, according to their appearance, as "strawberry marks," etc. They are usually present at birth, but often spread from a minute red spot to cover large surfaces. In its most usual form a cutaneous nævus forms a bright-red, sharply defined patch without obvious elevation of the surface, but at other times the affected part of the skin presents a somewhat velvety surface, or may be raised in the form of a soft nodular or warty growth of a dark-red or purple colour. The so-called "port-wine stains" on the face and elsewhere need no further description; the patch may be uniformly coloured, but sometimes, by putting the skin on the stretch, the small branching vessels can be recognized. In the case of a large hæmangioma the increased heat of the part is very obvious to the hand, and by pressure the colour of a nævus disappears more or less completely.

Cutaneous nævi are most common about the head and face. Of 1,600 nævi observed by Lewis Jones, 851 were situated on the head or face, 82 on the neck, 413 on the trunk, 229 on the limbs, and 25 in other situations. The same observer noticed that female children were about twice as often affected as males, whilst multiple nævi were four times as common in girls as in boys. Although not congenital, a common form of angioma on the face in children is the nævus araneus or "spider nævus," which consists of a minute raised red spot from which a number of fine red lines radiate.

Capillary nævi of the skin are not always entirely superficial, but may extend into the subcutaneous tissue, forming a soft tumour resembling a cavernous angioma in its characters; whilst frequently a nævus has a mixed structure, the cutaneous part being capillary and the subcutaneous part cavernous.

After reaching a variable size, cutaneous nævi usually remain stationary. They rarely disappear entirely, except the very faint nævoid patches which are so frequently present in the eyelids and adjacent parts in newly-born children. Occasionally a cutaneous nævus fades in the centre whilst it continues to spread at its margin. Nævi involving the skin sometimes ulcerate, and may shrink and become cicatricial as the ulcer heals. Ulceration occasionally leads to hæmorrhage which may be alarming.

be the source of repeated
r instance, from the nose,
of this nature the angioma

may be an isolated growth, but in other instances the telangiectases are multiple, and are present on the skin and mucous membranes.

These *multiple telangiectases* have been observed chiefly in females, and in some instances have been hereditary. In the case of a woman aged 56, recorded by Sidney Phillips, there had been attacks of epistaxis since childhood, and for eleven years occasional bleeding from vascular patches on the tongue, and there were small red nævoid spots on the skin of the trunk. The patient's father had suffered from bleeding from the nose and tongue, a sister died of bleeding from the gums, and one child had vascular patches on the tongue. In a similar case, also of a woman, recorded by Parkes Weber, there were angiomas on the face, ears, lips, tongue, conjunctiva, nose, pharynx, and epiglottis. There was also a retinal hæmorrhage in one eye, and there remained evidences of an old hæmorrhage in the other. The woman's mother and several of her children were similarly affected. Cases of this nature must be carefully distinguished from hæmophilia, which is probably exclusviely met with in males.

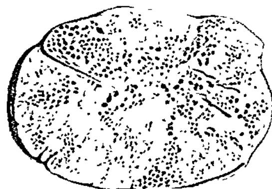


Fig. 67.—Cavernous angioma, in section. The tumour was situated beneath the temporal muscle.

After middle age it is very common to find small red spots on the skin, especially on the front of the trunk. The smallest, not larger than a pin's head, are flat, but when of somewhat larger size they may be distinctly raised. These spots were first described by Campbell de Morgan, who believed them to be especially common in the subjects of malignant disease, particularly carcinoma of the breast; hence they are known as "de Morgan's spots." They are certainly often seen in women with mammary cancer, but are quite common in both sexes, and appear to be of no significance. They are vascular in nature, consisting of thin-walled dilated cutaneous capillaries, and are probably the result of degenerative changes.

Cavernous angioma.—A cavernous nævus has the structure of erectile tissue. A section of such a tumour often presents, even to the naked eye, a finely-spongy structure of a deep-red colour (Fig. 67). In many cases the tumour is completely encapsuled, and the vessels which enter and leave it are not unusually large or numerous. Examined microscopically, a cavernous angioma presents

large blood-spaces or sinuses lined with endothelium, and lying in a cellular connective tissue in which bundles of smooth muscle-fibres are often present (Fig 68). The small cavernous angiomas, which are not uncommon in the liver, develop, according to Ziegler, in advanced age, and are not congenital. They are said to result from dilatation and coalescence of neighbouring capillaries within the lobules.

A cavernous hæmangioma, when situated in the subcutaneous tissue

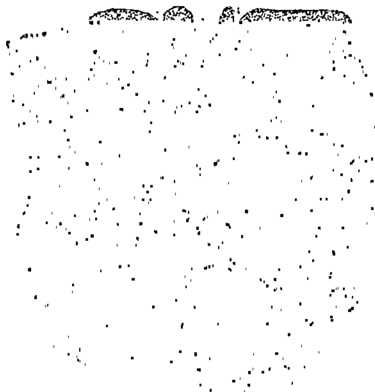


Fig. 68 —Microscopic section of a cavernous angioma, showing large spaces filled with blood and surrounded by a cellular connective tissue.

or other accessible situation, such as in the substance of the lip, forms a soft, spongy, purple tumour of well-defined outline and often with a lobulated surface The overlying skin or mucous membrane may be normal or the seat of a capillary nævus. The tumour often presents the peculiar feature that it can be considerably diminished in size by pressure, and that when the pressure is removed the tumour expands like a sponge as the cavernous tissue refills with blood. This sign is by no means always obtainable, especially if the vascular tissue

is largely mixed with fat or fibrous tissue. Occasionally the tumour pulsates, and often has an increased tension during a straining effort.

Plexiform angioma.—This rare form of angioma was formerly known by the names "cirsoid aneurysm" and "aneurysm by anastomosis." Although the vessels composing it are chiefly arterial, the veins and capillaries of the part may also partake in the production of the tumour, and thus the name "arterial angioma," which is sometimes applied to it, is not strictly accurate. The disease is most common in the scalp, especially in the distribution of the temporal and occipital arteries, and in the external ear. It consists of a mass of large, tortuous, intercommunicating, pulsating vessels, sometimes forming a tumour extending over a considerable area. At the peripheral parts of the mass the normal arterial trunks are much enlarged, and can be traced into it. Accompanying the pulsation a loud bruit may be audible to the patient as well as to the observer. The whole tumour has a convoluted surface and a bluish colour; the overlying skin may also be nævoid, and in the scalp generally becomes hairless.

Plexiform angioma usually develops gradually in young adults; it probably originates in a congenital nævus through an exaggerated formation of the enlarged and convoluted arterioles that sometimes form part of such a nævus. In other cases the disease has followed an injury.

Although most common on the scalp, plexiform angioma has been met with elsewhere. It has been known to occur in connexion with the cerebral arteries, and *has been recorded on the hands and feet.* Bland-Sutton mentions a case which came under his treatment in which a large tumour of this nature was situated in the perineum, the corpus spongiosum being surrounded by numbers of large vessels, some having the characters of arteries and others of veins. The disease has also been recorded in the orbit as a very exceptional cause of pulsating exophthalmos

A plexiform angioma tends to increase, often at an irregular rate, and may prove fatal from hæmorrhage, or from ulceration and septic complications.

It has already been remarked that cavernous angiomas are often wrongly termed venous, and also that in plexiform angiomas some of the component vessels may partake of the character of veins rather than arteries. True *venous angiomas* can indeed hardly be recognized as a distinct variety. In certain cases of varix, however, in which the venous dilatation occurs in early life, independently of any obvious venous obstruction, and is limited in its distribution, the condition may be regarded as rather of the nature of a vascular new growth

than as a mere varicose enlargement of a normal vein. The association of this variety of varicose veins with cavernous angiomas has occasionally been observed.

Angioma of the tongue.—Mention has been made of capillary nævi of the tongue, sometimes associated with multiple telangiectases of the skin and mucous membranes. Cavernous angiomas are sometimes met with in this situation as isolated spongy tumours in or beneath the mucous membrane, or in combination with lymphangioma in some cases of congenital macroglossia. In a specimen preserved in the Museum of University College Hospital the condition appears to be rather of the nature of a plexiform angioma. The right half of the tongue was removed by Barker from a man aged 34, in whom an enlargement of the part had existed since boyhood, and who had suffered repeated attacks of hæmorrhage resulting in intense anæmia. The bleeding occurred from a group of enlarged papillæ, but the whole of the right half of the tongue was soft and swollen. The right lingual artery and its branches were enlarged and tortuous, and beneath the mucous membrane was a plexus of dilated capillaries from which loops extended into the papillæ.

Angioma of the rectum.—Several cases of cavernous angioma of the mucous membrane of the rectum are on record. In one, brought before the Royal Medical and Chirurgical Society by Barker in 1883, a man aged 45 had suffered since boyhood from attacks of rectal hæmorrhage, which gradually increased in severity and eventually proved fatal. Examination of the rectum during life revealed the presence of three shallow ulcers, from which blood continuously oozed, and a peculiar purple mottling of the surrounding mucous membrane. The tumour, which had the typical structure of a cavernous angioma, involved the mucous and submucous layers of the left and anterior aspects of the bowel for a distance of 8·5 cm.

Angioma of bones.—Many cases formerly described as erectile tumours of bone were undoubtedly pulsating myelomas and sarcomas, and although a few examples of true angioma are on record they are extremely rare. Occasionally a nævus of the overlying soft parts may be intimately connected with and even involve the subjacent osseous tissue. In 1841 Liston recorded an extraordinary case of a large vascular tumour growing in connexion with the upper jaw, the specimen being preserved in University College Hospital Museum. The tumour, which has the typical structure of a cavernous angioma, grew from the posterior surface of the maxilla, filling the spheno-maxillary and lower part of the temporal fossæ and projecting into the pharynx and mouth. Frequent attacks of hæmorrhage occurred from the growth, and on excising the maxilla the whole of the lobulated tumour came away with it.

Angioma of muscle.—Cavernous angioma has been met with in muscles, chiefly those of the limbs, and may occur also in the deep planes of connective tissue. Fig. 67 shows such a tumour, removed by Christopher Heath from the temporal fossa, where it lay beneath the temporal muscle. In view of the fact that the tumour occurred in an adult who had only been aware of its existence for a comparatively short time, it is not surprising that its true nature was not suspected until it had been removed.

Angioma of synovial membranes.—Attention has been called by Eve to the occasional occurrence of angiomatous growths in connexion with the synovial membrane of joints, and the close resemblance which such a condition may bear to a localized tuberculosis. A case of this nature, strikingly similar to one of those recorded by Eve, has come under our observation. The tumour formed a somewhat ill-defined mass in connexion with the upper and outer part of the left knee-joint. In the skin over it was a scar, marking the site of an operation performed several years previously, the nature of which was not known. In view of the position of the swelling and its soft consistence, it was regarded as a localized tuberculous deposit in the synovial membrane, until an exploratory incision revealed the presence of a typical spongy angiomatous growth which involved the synovial membrane and the adjacent part of the vastus externus muscle.

Nævo-lipoma.—Fat may occasionally be present in the substance of an angioma in such amount that the tumour partakes of the characters of a lipoma rather than an angioma. Indeed, a tumour in a child having the character of a lipoma often proves on examination to be a nævo-lipoma.

The same combination is also met with in a diffuse form in certain cases of congenital enlargement of a limb. In some cases of this nature the enlargement is limited to the soft parts and is caused by a diffuse fatty and vascular growth.

Diagnosis of angiomas.—The nature of a cutaneous angioma is usually obvious, and the diagnosis is rarely difficult in the case of a subcutaneous angioma in a young child. It may, indeed, be laid down as a useful rule that in discussing the nature of an obscure tumour in a child, the possibility that it is an angioma is generally deserving of consideration. On the other hand, an angioma first observed in adult life, and situated in some unusual situation, may present no features by which its true nature can with any certainty be determined. Mention must be made of the possibility of mistaking a nævus of the scalp situated over one of the fontanelles, or at the root of the nose, for a meningocele; while the not uncommon presence of a capillary nævus in the skin over a meningocele may

lead to the more serious mistake of regarding the subcutaneous tumour as a nævus also.

Treatment.—In a young child a small cutaneous nævus which is not increasing may be left untreated in the hope that it will gradually fade. With the slightest sign of increase, especially on the face, treatment should at once be adopted. In situations where a linear scar is of no importance, excision is the best treatment, but in conspicuous situations the nævus may best be treated by multiple punctures with a very fine galvano-cautery, the margin being especially attacked, or by carbon dioxide snow. The small spider nævus of the face is best destroyed by electrolysis, the needle being introduced into the small central spot.

All methods of treating large " port-wine stains " on the face have hitherto proved very disappointing, but some improvement may follow the use of radium

Nævi involving both skin and subcutaneous tissue may be treated by excision, electrolysis, or the galvano-cautery. The excision of cavernous angiomas may be safely performed, provided that the incisions be kept outside the capsule of the tumour. The vessels then divided are not numerous and are small in size, whereas if the incision accidentally wounds the cavernous tissue the hæmorrhage may be alarming. Large subcutaneous nævi have been successfully treated with radium

A plexiform angioma may sometimes be dealt with by excision. When, however, the condition involves a large area, such as the temporal region, ligature of the supplying vessels at the periphery of the tumour has seemed to yield the best results

LYMPHANGIOMA

Lymphangioma, or lymphatic nævus, occurs in two forms, the capillary and the cavernous, which differ only from the corresponding varieties of hæmangioma in the nature of the contents of the vessels or spaces Three distinct conditions may result from the presence of a lymphangioma · (1) Vesicles on a cutaneous or mucous surface; (2) a multilocular cystic tumour or cystic hygroma; (3) a localized enlargement of the affected part, such as the tongue or lip. In some instances it may be difficult to decide whether a given lymphatic dilatation is to be regarded as a true lymphangioma, or as the result of a lymphatic obstruction. Thus, in some forms of obstruction, dilated lymphatic vessels or lymphangiectases may result; and again, certain forms of local hypertrophy or elephantiasis are the result of a chronic lymphatic obstruction and not of a true lymphangiomatous growth.

Simple capillary lymphangiomas of the skin and mucous membranes

are very rare. In the conjunctiva small tumours of this nature are sometimes present in the form of rows of minute clear vesicles like tiny pearls. In the skin a *similar condition* has been described in the form of groups of small vesicles from which a clear fluid escapes on puncture.

Cavernous lymphangioma is represented by the not very un-



Fig. 69.—Cystic hygroma of neck and axilla.

common cystic tumour met with in the neck and elsewhere, and often known as the "cystic hygroma" (Fig. 69). The tumour is congenital, but, *like other forms of angioma, often increases considerably* after birth. It forms a lobulated mass, frequently of large size, and covered with normal skin, through which the lymph-containing cysts appear of a bluish colour. It consists of a mass of cysts held together by

connective tissue containing fat (Fig. 70) The varying characters of these tumours depend upon the size of the cysts and the amount of solid tissue present. The latter is found on microscopic examination to be intersected by dilated and cystic lymphatics. Sometimes one or more cysts may be of such a size as to form the bulk of even a large tumour. In some cases the tumour has a mixed structure, being partly hæmangiomatous and partly lymphangiomatous. The limitation of these cystic tumours is usually ill-defined, and the lymphatic growth may extend among the muscles and other deep structures. This fact is of great importance in considering the question of operation, especially when the tumour occupies the neck, for the removal is hardly likely to be complete, and the operation may be accompanied by very free bleeding.

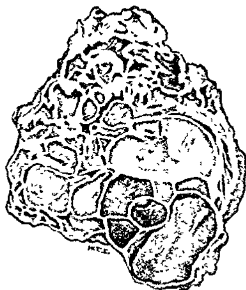


Fig. 70.—Cystic lymphangioma of axilla.

Hutchinson was, we believe, the first to point out that these tumours are liable to recurrent attacks of inflammation. During these attacks the tumour increases in size, the overlying skin becomes reddened, and a well-marked febrile disturbance occurs. In a case which came under our notice, several attacks of this kind occurred, and in one of the most severe of these a medical man, who was unfamiliar with the condition, was narrowly prevented from treating the case as one of abscess of the neck As a matter of fact, the inflammation nearly always subsides without suppuration and may be followed by considerable shrinkage of the tumour. The causation of this intermittent inflammation has been studied by Riedel and Küttner. Among 19 cases of lymphangioma observed by Kuttner in Bruns's clinic, inflammation was noted 5 times—thrice in the tongue, once in the lip, and once in the wall of the thorax. Küttner believes the inflammation to be due to an infection of the lymph spaces of the tumour either directly from the surface or by way of the lymphatics. In the case above mentioned, one at least of the attacks of inflammation followed the occurrence of sore throat.

Lymphangioma of the tongue may occur as a localized patch in which the papillæ are enlarged, and may be transformed into small vesicles as the result of dilatation of the lymphatic vessels. The more important variety is the *diffuse form, which is the most* common cause of congenital enlargement of the tongue, or *macroglossia*. The enlargement, although usually noticeable at or soon after birth, may gradually increase until a considerable part of the

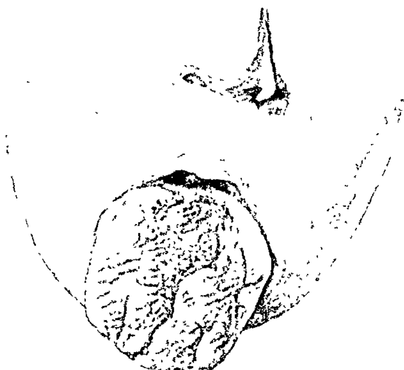


Fig. 71.—Congenital macroglossia, the result of diffuse lymphangioma. The surface of the tongue is deeply furrowed and presents enlarged cystic papillæ.

organ hangs from the mouth. The surface is usually irregularly fissured and the papillæ are enlarged (Fig. 71). From constant irritation the condition is likely to be modified by inflammation.

Microscopic examination reveals the presence of dilated and cystic lymphatics in the mucous membranes, submucous tissue, and muscular substance; and Butlin refers to several recorded cases in which this variety of macroglossia was associated with other forms of lymphangioma, as, for instance, in the neck and floor of the mouth.

Treatment of lymphangioma. — A lymphangioma of moderate size may be treated by excision. The difficulty of treating

in this way the large cystic lymphangiomas of the neck has already been mentioned, and in considering the question of operation the tendency of these tumours eventually to shrink must be taken into account. Lymphangiomatous macroglossia has often been successfully treated by excising a wedge-shaped portion of the front of the tongue.

ENDOTHELIOMA

An endothelioma is a tumour the essential elements of which are endothelial cells lying in a connective-tissue stroma; and it must be

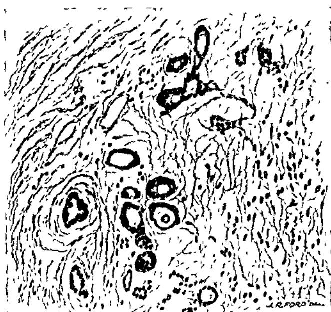


Fig. 72.—Microscopic section of endothelioma (parotid tumour).

assumed that such a tumour has its origin in the endothelium of the blood- and lymph-vessels and spaces or in that covering the surface of serous membranes.

Much difference of opinion exists concerning the frequency with which these tumours occur, and, indeed, Nicholson, after a careful consideration of the subject, is inclined to deny their existence. Without taking this extreme view, much care is needed in labelling a tumour as endothelioma, and it is necessary to state clearly the grounds on which such a conclusion is based. Kettle and Ross are of opinion that only those tumours can safely be regarded as endotheliomas in which the formation of lumina by the vacuolation of

the tumour-cells in a manner similar to that occurring in the normal formation of capillaries can be demonstrated. It may be doubted, however, whether such a distinction is not too exclusive.

In connexion with tumours of an endothelial structure, a difficulty arises in the fact that while some of them present the characters of benign growths, others assume evidences of malignancy and have the characters of a sarcoma. Tumours of the latter group will be



Fig. 73.—Microscopic section of endothelioma (parotid tumour).

found described among the malignant growths as "endothelial sarcomas" (p 515).

Microscopic structure.—In the most common form of endothelioma the striking histological feature is the presence of spaces lying in a connective-tissue stroma and lined or filled with cells The *cells lie in actual contact one with another, and whilst in some spaces* they form a single layer and are flattened in shape, in others the cells are spheroidal or polygonal, and partially or completely fill the lumen. *The spaces may thus closely resemble in section an embryonic vessel,* being merely tubular clefts surrounded by flattened cells (Fig. 72), whilst if the lining cells assume a spheroidal or polygonal form the *resemblance to a glandular structure may be very close* (Fig. 73). By a further proliferation of the cells a plexiform arrangement of



Fig. 74.—Microscopic section of endothelioma (parotid tumour).



Fig. 75.—Microscopic section of endothelioma of ovary.

(From a case under the care of Herbert Spencer)

threads of cells may be produced (Fig. 74), or large irregular cell masses may result, in the centre of which the lumen persists merely in the form of a slit-like cleft. Lastly, the cell growth may result in the formation of solid cell masses and strands in which all evidence of a central lumen is lost, and in which the true nature of the tumour is only evidenced by the continuity that can be traced between the solid cell masses and others in which a lumen is present (Fig. 75).

The stroma of endotheliomas varies much in both character and amount. It may be composed of dense fibrous tissue, or of soft, richly



Fig. 76.—Microscopic section of endothelioma of dura mater.

cellular tissue, but in some tumours it is largely myxomatous or hyaline (Fig. 74).

From the above short description of the chief histological features of an endothelioma it will readily be understood that the resemblance to other forms of new growth may be very close. Thus, in some tumours of this class the structure is closely allied to that of an angioma; in others the appearances may be confused with those of an epithelial tumour; whilst in yet another form the cell proliferation may be so marked as to produce a structure difficult to distinguish from that of an undifferentiated sarcoma.

Endothelioma of the meninges (Fig. 76).—This is met with as a slowly growing encapsuled tumour originating in the dura mater, most commonly in the frontal region. On its deep aspect

the tumour compresses without invading the brain, while superficially the tumour may affect the skull. In some cases the bone is progressively thinned, whilst in others it may be thickened, so as to produce a hemispherical osseous tumour. In accessible regions the tumour is favourable for removal.

A special variety of endothelioma of the meninges is represented by the tumour to which Virchow applied the name "psammoma" or "sand-tumour." This name was suggested by the peculiar gritty surface sometimes presented by a section of the growth, and due to small calcareous deposits. Microscopic examination shows that the tumour is mainly composed of fibrous tissue and that the calcareous deposit occurs in the form of round, concentrically laminated bodies closely resembling corpora amylacea in appearance. In some of these bodies it is possible to recognize the flattened, nucleated cells from which they arise. Psammomas are usually of small size, and may be single or multiple. They are as a rule unproductive of symptoms, but occasionally, especially in the spinal cord, they cause pressure, and have been removed by operation.



Fig. 77.—Endothelioma of parotid region.
(From a case at University College Hospital.)

Mixed tumours of the parotid region and neighbourhood. — This group of tumours is most commonly represented by the well-known "parotid tumour," but others of essentially the same nature are met with in the submaxillary region, lip, palate, and orbit.

The parotid tumour generally presents itself as a circumscribed, lobulated, slowly growing tumour, which usually lies superficially to some part of the parotid gland, often immediately below the lobule of the ear. The tumour may reach a very large size without showing any evidence of malignancy (Fig. 77).

Tumours in all respects similar to the parotid tumours are occasionally met with in the submaxillary region. The tumour of

the lip, from which the section illustrated in Fig. 78 was made, was removed by Liston. It was of ten years' growth, and formed a rounded circumscribed tumour, 12 mm. in diameter, embedded in the substance of the lip.

Similar encapsuled tumours are also occasionally found in the palate. *In a case recorded by Christopher Heath*, a tumour of this



Fig. 78.—Microscopic section of chondro-endothelioma of lower lip.

nature was removed from a woman aged 48, in whom it had existed since childhood.

Examined microscopically, tumours of this group vary much in structure, and may be composed, in varying degrees, of fibrous tissue (sometimes hyaline), myxomatous tissue, and hyaline cartilage, any one of which may preponderate; angiomatous tissue may also be present. In addition to these tissues, certain cell-formations are always present, and may be arranged so as to surround lumina or to form a network of cell-threads or columns (Figs. 72, 73, 74). There is

still a wide divergence of opinion concerning the nature of these cells. Some pathologists regard them as epithelial, and consequently classify the tumours as adenomas or carcinomas The view is here taken that the structure is that of an endothelioma The varying structure of these tumours accounts for the wide differences in the naked-eye appearance of the growth. Sometimes it is firm and fibrous, at others soft and gelatinous, whilst if cartilage is abundant it may be bluish-grey and semitranslucent like a pure chondroma. The presence of cartilage is probably explained by the derivation of the tumours from the indifferent mesoderm from which the branchial arches are developed.

The endotheliomas of the parotid and neighbouring regions, although they may pursue an absolutely benign course extending over many years, may eventually extend into the surrounding tissues and exhibit very marked evidences of local malignancy. Such an altered mode of growth may be considered to result from the transformation of a simple endothelioma into an endothelial sarcoma.

In 1888, Hutchinson described a peculiar form of "potato-like" tumour which he had observed in several cases in the upper part of the neck beneath the sterno-mastoid. It is probable that these tumours are identical with those regarded by several observers as originating in the carotid body, and usually considered as endotheliomatous in nature.

Endotheliomas are also described in the tongue, uterus, testicle, and ovary, but some of the tumours in these and other situations, such as the bones, should be regarded rather as endothelial sarcomas.

MYOMA

A myoma is a tumour composed of striped (rhabdo-myoma) or unstriped (leio-myoma) muscle-fibres.

RHABDO-MYOMA

A tumour composed entirely of transversely striated muscular tissue has not yet been described, and it is probable, as suggested by Bland-Sutton, that certain elongated and transversely striated cells occasionally seen in spindle-celled sarcomas are not really muscle-fibres. Striated muscle-fibres are, however, sometimes present in certain mixed tumours of the kidney and the testicle, occurring in early life

Shattock has drawn attention to four specimens of polypoid tumours of the lower part of the bladder, in all of which striped muscle-fibres are present. Three of the specimens are in the Museum of the Royal College of Surgeons, and one in the Museum

of St. Thomas's Hospital. In three the bladder is that of a young child, and in all it is probable that the tumour was congenital. Shattock suggests that such a tumour, occurring in a position where voluntary muscle is not normally present, is the result of displacement or heterotopia, and develops from cells concerned in the formation of the external sphincter of Henle, which have abnormally extended or have been displaced into the subepithelial tissue of the bladder.

LEIO-MYOMA

Tumours composed of unstriped muscular fibres mixed with a varying proportion of fibrous tissue (fibro-myoma) are chiefly met

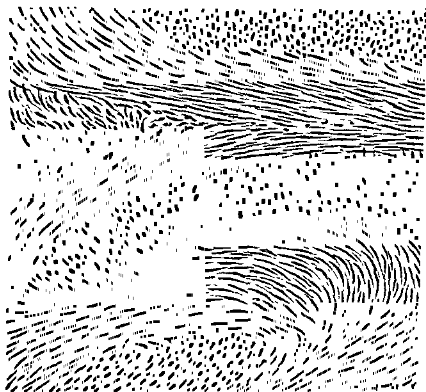


Fig. 79.—Microscopic section of fibro-myoma of uterus.

with in the uterus, but occasionally occur in the wall of the alimentary canal and in the skin.

Examined microscopically, the muscle-cells are slender, elongated and fusiform, and the nuclei are rod-shaped and often sinuous. The muscle-cells are arranged in fasciculi which intersect in various directions, and when the cells are seen in transverse section they appear as rounded or polygonal clear areas, in the centre of many of which the nucleus is seen as a dark spot (Fig. 79). Between the muscle-cells is

a variable, but usually small, amount of fibrillated connective tissue, which becomes evident in a section stained by van Gieson's method, the muscle cells staining yellow with picric acid, and the fibrous tissue red with fuchsin. In some fibro-myomas, especially young tumours, it may be difficult to distinguish the cells from those of a spindle-celled sarcoma, but usually the latter are less uniform in shape and size, and arranged in less regular fasciculi.

Fibro-myoma of the uterus.—Fibro-myomas or "fibroids" of the uterus are extremely common, and may be single or multiple.

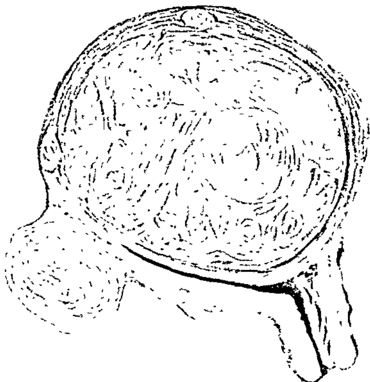


Fig. 80.—Fibro-myomas of uterus, intramural and subserous.

According to their position, the tumours may be subserous, intramural, or submucous; they are usually rounded in shape and lobulated on the surface, and may reach such an enormous size as to constitute some of the largest tumours met with in the human body. The submucous variety frequently assumes a polypoid form, and the subserous tumours are also often pedunculated. On section, a fibro-myoma of the uterus presents an appearance closely resembling that of a fibroma, the cut surface being marked by whorls and intersecting tracts of a glistening white colour (Fig. 80) Except when small, the tumour possesses

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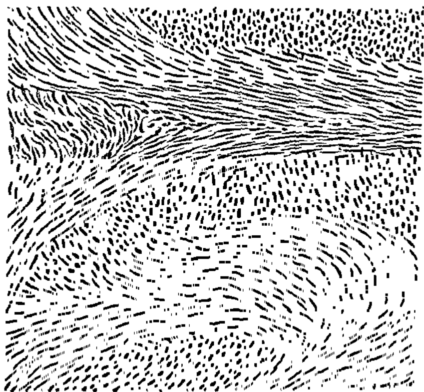


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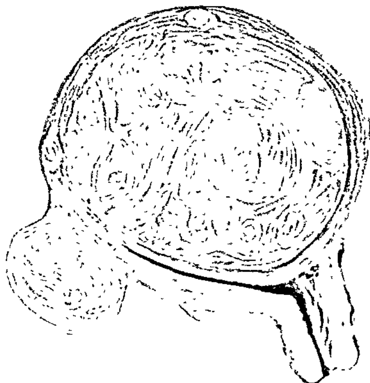


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a distinct fibrous capsule, and can be readily enucleated. On the cut surface of the tumour are often seen a few large veins, the walls of which cannot collapse on account of their intimate connexion with the tumour substance. These veins are frequently connected with an abundant plexus on the surface of the uterus, which may be a source

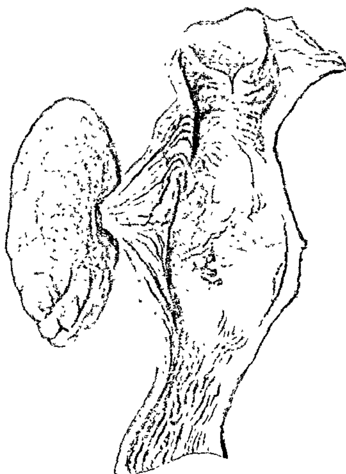


Fig. 81 —Submucous fibro-myoma of œsophagus. The œsophagus has been laid open from behind and the tumour attached to the mucous membrane turned outwards.

of free hæmorrhage during operation. Uterine myomas often undergo atrophy after the menopause and after the removal of the ovaries.

Modifications of structure.—Among the most important degenerations to which myomas of the uterus are liable are the so-called hyaline, the mucoid and calcareous, and "red degeneration"—a condition of no practical significance, in which the tumour substance has a dark-red colour, probably due to imbibition of colouring matter from the blood. In the hyaline degeneration the change affects the

fibrous tissue, which becomes swollen and homogeneous in appearance, and there may be wide separation of the fasciculi of muscle-cells, without producing any great change in the naked-eye characters of the tumours. Mucoid degeneration is very common in scattered areas of these tumours, but may advance to such a degree as to result in extensive cystic formations ("fibro-cystic tumours"). Calcareous deposits may be limited to parts of the tumour, or may be so extensive that the tumour is almost entirely converted into a stony mass.

Among other changes to which these uterine tumours are liable may be mentioned suppuration and, in the case of submucous myoma, sloughing and gangrene. Subserous tumours occasionally become hæmorrhagic as the result of torsion of the pedicle. Finally, it is an important fact that a fibro-myoma of the uterus may undergo a sar-



Fig. 82.—Microscopic section of neuroma.
(*From Knauss's case, Virchow's Arch., vol.* cliii., 1898.)

comatous transformation. This may occur without, in the early stages, any striking change in the gross features of the tumour, but later the affected part presents a homogeneous and wax-like appearance.

Fibro-myoma of the alimentary canal.—Fibro-myomas of the alimentary tract may project beneath the mucous membrane or the serous coat. In Fig. 81 is illustrated a large submucous fibro-myoma of the œsophagus, which had occasioned such extensive pressure necrosis of the œsophageal wall as to lay bare some of the cartilaginous rings of the trachea. The tumour had caused dysphagia, which was thought to be the result of malignant disease of the œsophagus, and for which gastrostomy was performed.

Numerous cases of fibro-myoma of the stomach are on record, in several of which the tumour, even though of small size, occasioned

pyloric obstruction. Small, simple polypi of the intestine may belong to this class of tumours, and are of clinical importance chiefly as an occasional cause of intussusception.

NEUROMA

It has already been pointed out that the term neuroma is sometimes applied to tumours of nerves independently of their structure. It should, however, be reserved for tumours composed of nerve-tissue, which, in view of the fact that ganglion-cells are present, are sometimes termed "ganglio-neuromas."

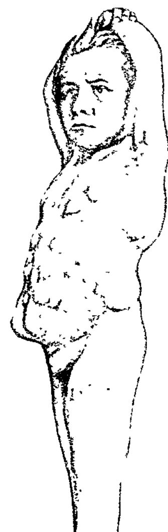


Fig. 83.—Multiple neuromas.
(*Knauss, Virchow's Arch., vol.* cliii., 1898.)

Tumours of this nature are not so rare as was formerly thought. They contain nerve-fibres, occasionally medullated, and ganglion cells of the type of those found in the sympathetic. The tumours, which in some situations, such as the mesentery, have been known to reach the size of a coco-nut, present to the naked eye an appearance similar to that of a fibroma or fibro-sarcoma. They are usually encapsuled, and pursue a benign course. These tumours usually occur in connexion with the main sympathetic cord or plexuses, and have been met with in the neck, thorax, and abdomen. In the latter situation they have been found in the retroperitoneal tissue or between the layers of the mesentery, as well as in connexion with the medulla of the adrenal. They may also occur in the central nervous system and skin.

In Knauss's case, a girl aged 8, multiple subcutaneous tumours, varying in size from a pea to a small orange, were present on the trunk and thighs, and were thought to be lipomas (Fig. 83). Some were removed, and on section presented a homogeneous, light-yellow, transparent appearance, with white fibrous streaks running irregularly through their substance. (Fig. 82.) From the structure of the tumours, and their connexion with blood-vessels, Knauss concluded that they originated in the minute ganglia in the sympathetic fibres accompanying the blood- and lymph-vessels.

The bulbous enlargements which form on the ends of nerves that have been accidentally wounded in their continuity or divided in amputation are sometimes spoken of as "division" or "amputation neuromas." A certain degree of bulbous enlargement may in these circumstances be regarded as normal, and even when the bulb reaches an excessive size it cannot justly be viewed as a tumour.

A section through the bulbous end of a divided nerve shows microscopically bundles of newly formed nerves irregularly arranged and lying in a stroma of fibrous tissue. The formation of nerve-fibres must be regarded as evidence of a disturbed attempt at repair.

ADENOMA

An adenoma is a simple tumour corresponding in its structure more or less closely with that of a secreting gland, and consisting of epithelium-lined spaces lying in a connective-tissue stroma. The histological characters of an adenoma are necessarily dependent upon those of the part in connexion with which it arises. Accordingly, four types of adenoma may be recognized—racemose, tubular, cystic, and solid. The racemose adenoma is exemplified by the simple glandular tumours of the mamma, in which, as will be seen, branching ducts and acini are present. The simple polypus of the rectum is the best example of a tubular adenoma. The cystic variety is seen in tumours of the ovary and thyroid gland, and the solid variety in those of the adrenal In addition to the adenomas which arise in close association with normal glands, others are occasionally met with, which probably owe their origin to some vestigial structure. For example, certain tumours of glandular structure occurring in the vaginal fornix probably arise in vestiges of the duct of Gartner.

Before proceeding to a description of the more common forms of adenoma it is necessary to point out that some confusion has arisen from the application of the term "adenoma" to various glandular hyperplasias which do not partake of the nature of true tumours. For instance, in the chronic inflammatory hyperplasia sometimes affecting the integument of the nose (rhinophyma), the large sebaceous glands of the part form such a predominant histological feature that the condition has sometimes been termed a sebaceous adenoma, although it possesses none of the characters of a tumour-formation. Again, in certain chronic inflammations of the gastric and intestinal mucous membrane, localized glandular overgrowths are not uncommon and are sometimes wrongly regarded as adenomas. Further, in the chronic enlargement of the prostate a number of closely packed glandular masses are frequently present, but in view of the fact that there is strong evidence for regarding the enlargement as

inflammatory and not a tumour-formation, these *glandular deposits* should not be termed adenomas.

Considerable difficulty is sometimes encountered in endeavouring to decide whether a tumour is of the simple glandular (adenoma) or malignant glandular (carcinoma) type. This difficulty arises from the fact that in their histological structure certain carcinomas retain in a striking degree a close resemblance to the gland in which they arise, as, *for instance, in certain malignant tumours of the* thyroid. The distinction must be based not only on the histological structure, but also on the relations of the tumour elements to the surrounding tissues. For instance, many carcinomas of the large intestine consist of spaces lined with a very regular layer of columnar epithelium, closely reproducing the structure of the normal intestinal glands. The adenomas of the intestine present *similar epithelium-lined spaces, but the two classes of tumour differ* essentially in their relations to the surrounding tissues. The gland-like structures of the carcinoma extend to the deeper parts of the intestinal wall, and are found invading the muscular coat, whereas in the adenoma the epithelium-lined spaces are confined to the mucous membrane in the normal situation of the glands.

Adenoma of the breast.—Adenoma, the most common *simple tumour of the mammary gland,* is *of several varieties, the* differences arising from modifications of the glandular spaces or connective-tissue stroma. A constant feature is the presence of a perfect capsule surrounding the tumour and rendering it capable of removal by enucleation. The breast itself either remains in a perfectly normal state, or, if the tumour is large, is displaced, and may become flattened out over its adjacent surface In the large majority *of cases the tumour lies on the surface or at the margin of the breast,* to which it has only very loose connexions, suggesting that it has arisen in a small outlying fragment of glandular tissue which has failed to become connected with the general glandular apparatus. In rare instances a typical adenoma is embedded in the breast tissue, and occasionally tl [illegible] certain glandular cysts of the breast [illegible] The perfect encap*sulation of an* adenoma explains the considerable degree of mobility beneath the skin, and independently of the breast, which is often its most striking clinical feature

Adenomas of the breast are most common in young women between the ages of 20 and 30, and are occasionally *multiple. The following* varieties deserve separate consideration :—

1. *Pure adenoma,* in which the structure closely resembles that of the normal gland, except that no large ducts are present and the stroma is devoid of fat.

2. *Hard fibro-adenoma*, in which the stroma is relatively abundant and consists of dense fibrous tissue.
3. *Soft fibro-adenoma*, in which the stroma is also abundant, but consists of richly cellular connective tissue.
4. *Cystic adenoma*, in which the glandular spaces become transformed into cysts of varying size, and are often occupied by intracystic growths.

1. The pure adenoma is very rare. A specimen in University College Hospital Museum was removed by Quain from a

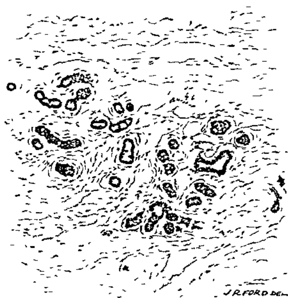


Fig. 81.—Microscopic section of hard fibro-adenoma of breast.

woman aged 26, and weighed 4 lb. In section the tumour closely resembles the pancreas in its naked-eye appearance, and the microscopic structure is like that of the normal breast, except that no large ducts are present and the fibrous stroma is free from fat.

2. The hard fibro-adenoma, on the other hand, is very common. To the naked eye the tumour usually presents the appearance of a lobulated fibrous growth of an opaque white colour, although, by examination of the cut surface with a lens, fine cleft-like spaces may often be detected in it. Examined microscopically, the tumour consists of epithelium-lined spaces widely separated by a dense fibrous stroma which is often arranged more or less concentrically around

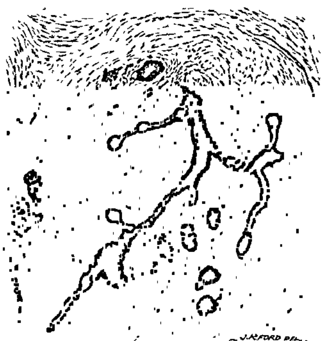


Fig. 85.—Microscopic section of hard fibro-adenoma of breast.

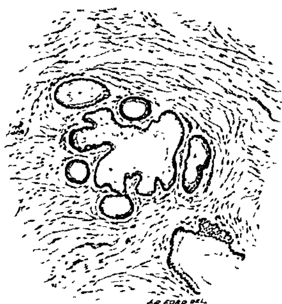


Fig. 86.—Microscopic section of hard fibro-adenoma of breast.

them. The spaces may resemble isolated acini or groups of acini communicating by small ducts (Figs. 84 and 85), or they may be transformed into small cysts (Fig. 86) or narrow, irregularly branching clefts (Fig. 87). The spaces are lined with epithelium of a polygonal or cubical shape.

3. The **soft fibro-adenoma** differs from the hard variety only in the character of the stroma, which may be so richly cellular as to suggest a sarcomatous change (Fig. 88). This variety of adenoma,



Fig. 87.—Microscopic section of hard fibro-adenoma of breast.

although it may increase rapidly and reach a large size, shows no true evidences of malignancy, and the name "adeno-sarcoma" which was formerly applied to it is very misleading.

4. In the **cystic adenoma** the glandular spaces of the tumour become transformed into cysts of large size which are occupied by foliaceous intracystic growths. These closely packed growths often give to a section of the tumour a very characteristic appearance which was aptly compared by Virchow to the centre of a split cabbage (Fig. 89). The true nature of the tumour will always be apparent on microscopic examination, which will show a transition from the typical structure of a fibro-adenoma to that in which the cystic transformation is very pronounced (Fig. 90).

The cystic adenoma often presents an extreme degree of lobulation, and in such tumours the opening up of one of the superficial cysts as the result of thinning and ulceration of the overlying skin may produce a misleading appearance of malignancy, especially if an intra-



Fig. 88.—Microscopic section of soft fibro-adenoma of breast.



Fig. 89.—Cystic fibro-adenoma of breast, in section, showing "split cabbage" appearance resulting from closely packed intra-cystic growths. The tumour is protruding through the skin.
(*University College Hospital Museum.*)

cystic growth should protrude from the ulcerated opening in the cyst. It is, however, necessary to insist upon the benign nature of this tumour, which was at one time known as a "cysto-sarcoma."

The cystic adenoma must be clearly distinguished from certain forms of cystic disease of the mamma in which the cysts are occupied by intracystic growths. In the one the cysts form part of an encapsuled tumour; in the other the cystic change affects the breast tissue itself, and no separate tumour is present.

The evidence that a carcinoma of the breast may take its origin from a simple adenoma is very scanty. The same breast may un-



Fig. 90.—Microscopic section of cystic adenoma of breast.

doubtedly contain both tumours, even in immediate apposition, but we know of only one specimen which suggests that the carcinoma had arisen from the adenoma (*see* Vol. II., p. 54)

Adenoma of the thyroid may in its structure resemble the developing or fully developed gland, and occurs as an encapsuled tumour over which the adjacent part of the gland is often stretched as a thin layer. An adenoma having the structure of the developing gland is characterized by the absence of colloid material, and on section presents a homogeneous substance of a whitish colour. The fœtal gland consists of anastomosing solid cylinders of cells lying in a vascular connective tissue, and, similarly, a section of this form of adenoma presents the appearance of alveoli filled with spheroidal cells and

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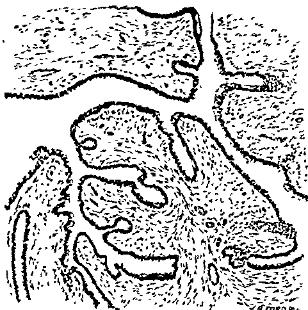


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separated by connective tissue with large, thin-walled capillaries (Fig. 91). Berry states that he has never removed an adenoma of this kind larger than an orange.

An adenoma having a structure like that of the fully developed gland consists of spaces lined with a low cubical epithelium and filled with colloid substance (Fig. 92). The spaces are usually larger than in the normal gland, and to the naked eye, or with very slight magnification, the tumour presents a fine meshwork, the spaces of which are filled with yellowish-brown, semitranslucent substance. The central part of such a tumour often presents an opaque fibrous



Fig. 91.—Microscopic section of adenoma of thyroid (fœtal type).

area sending radiations towards the surface (Fig. 93), and sometimes undergoing calcification.

In this variety of thyroid adenoma gross cystic changes are common, and thus by the coalescence of adjacent spaces even a large tumour may be converted into a single cyst in which the adenomatous tissue remains only as a thin layer on the inner surface of the fibrous capsule. An adenoma may undergo a rapid increase in size as the result of hæmorrhage into it.

Colloid adenomas may be single or multiple, and, especially when multiple, are often associated with a varying degree of general parenchymatous enlargement of the gland. It is indeed doubtful whether in such cases the multiple adenomas should be regarded as true tumours,

or as masses of glandular tissue which have gradually become isolated and encapsuled.

The removal of an adenoma of the thyroid has usually been per-

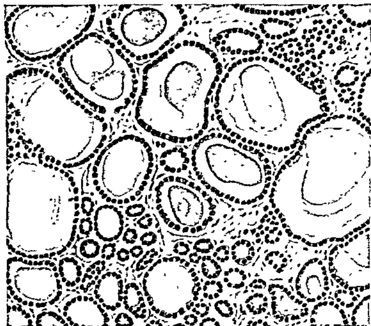


Fig. 92.—Microscopic section of colloid adenoma of thyroid.

formed by enucleation after dividing the thin layer of gland tissue lying over it. Berry, however, advises that simple enucleation should be reserved for quite small superficial tumours, and is of opinion that, as a rule, it is preferable to resect the tumour with the layer of gland tissue covering it, thus more certainly avoiding venous hæmorrhage or injury to the recurrent laryngeal nerve. In multiple adenomas associated with parenchymatous enlargement, partial extirpation is necessary.



Fig. 93.—Colloid adenoma of thyroid, in section.

Adenoma of the stomach and intestines.—Adenomas of the gastric and intestinal mucous membrane, although at first

sessile, tend, like all simple tumours of these parts, gradually to become *pedunculated*, and thus form one variety of simple polypus. They have a glandular structure corresponding to that of the part in which they arise, and frequently present a *more or less* papillary surface, so that it is difficult to draw a sharp line of *distinction between the adenomas* and papillomas.



Fig. 94.—Microscopic section of adenoma of rectum.

Adenoma of the stomach is rare. The tumour usually occurs in the region of the pylorus, and Mayo Robson and Moynihan quote cases in which an adenoma has been successfully removed for the relief of pyloric obstruction. When the growth is sufficiently large to form an abdominal tumour, the latter is characterized by its extreme mobility.

Adenoma of the intestine is also not common, and its practical importance chiefly concerns its tendency, like other simple tumours

of the bowel, to occasion intussusception. In the case of a woman admitted to University College Hospital, a pedunculated adenoma was removed from the sigmoid colon. The only symptom was rectal hæmorrhage, and a tumour which could be felt in the abdomen was suspected to be a malignant growth in the large intestine. An exploratory operation proved the abdominal tumour to be the misplaced left kidney, lying at the pelvic brim. In the sigmoid colon a round tumour was felt, which could be moved along the bowel for several inches. It was readily removed through an incision in the bowel, after ligaturing the long, slender pedicle.

Adenoma of the rectum occurs as the simple polypus not uncommon in young children. It forms a soft, red, pedunculated tumour, rarely larger than a small cherry. The pedicle may be sufficiently long to allow the tumour to protrude from the anus during defæcation, and spontaneous separation is probably more common than is supposed Prolapse of the whole circumference of the rectal wall may be caused by traction of the tumour. A few instances of large adenoma of the rectum in the adult are on record, but such cases are much less common than those of simple papilloma (p. 481). A section of one of these little tumours shows a number of epithelium-lined tubes resembling Lieberkuhn's follicles. In the centre is a radiating core of delicate connective tissue, and amongst the follicles small lymphoid nodules are often present (Fig. 94).

Adenoma of the umbilicus.—This is not uncommon in infants, and forms a small pedunculated tumour like a red currant. It causes a slight muco-purulent discharge, and is readily brought into view by everting the folds of the umbilicus. It can be removed by applying a ligature to the pedicle, or by dividing the latter with the point of a fine cautery. Occasionally a tumour of this nature is associated with the presence of a fæcal fistula. The structure of these tumours, which is identical with that of adenoma of the rectum, is illustrated in Fig 95

The tumour doubtless arises in connexion with the outer extremity of the vitelline duct. In one recorded case a tumour of the umbilicus, similar in appearance to an adenoma, proved to be a simple angioma. Adenomatous tumours of the umbilicus are occasionally met with in the adult.

Adenoma of the kidney.—Small white or yellow nodules are occasionally seen in the cortex of the kidney. They have the structure of papillary adenomas, and may readily be mistaken for adrenal rests (p. 586).

Adrenal adenoma.—Small tumours, usually rounded in shape, are not uncommon in the suprarenal body. They are yellow in colour, and usually have a structure resembling that of the zona fasciculata,

consisting of solid columns of polyhedral cells containing fat, and separated by a delicate, scanty stroma composed chiefly of thin-walled capillaries.

The very interesting fact may here be noted that numerous cases are on record in which the presence of a tumour of the adrenal, usually, however, of a malignant type, has been associated with an extraordinary degree of precocious sexual development. These will be referred to subsequently (p. 588).

Adenoma of the uterus.—A *fibro-adenoma* of the mucous membrane of the body of the uterus occurs as one form of simple



Fig. 95.—Microscopic section of adenoma of umbilicus.

polypus, but is much less common than the mucous polypus and the pedunculated submucous fibro-myoma. The tumour is usually small, and consists of spaces lined with cubical epithelium lying in a connective-tissue stroma.

Certain tumours of the uterus, consisting chiefly of muscular and fibrous tissue, contain, however, such a considerable amount of glandular tissue in the form of spaces lined with cubical epithelium as to justify the name "adeno-myoma" being applied to them. To the naked eye such a tumour does not necessarily present any features distinguishing it from an ordinary fibro-myoma, but occasionally the glandular elements may become dilated into cysts so as to convert the whole tumour into a lobulated cystic mass. An adeno-myoma of the uterus may, if it reaches a large size, extend into the broad ligament, but tumours of a similar nature may originate in this situation, probably in the remains of the Wolffian body or duct.

The name adeno-myoma, or "diffuse" adeno-myoma, is also applied to another condition in the uterus, in which the whole or a part of the cavity of the body is surrounded by a thick layer, consisting of the hypertrophied glands and stroma of the mucous membrane intimately mixed with tracts of fibro-muscular tissue. Tumours having the structure of a uterine adeno-myoma are occasionally found beyond the limits of the uterus, as for instance in the groin, abdominal wall, recto-vaginal septum and sigmoid colon. In the two latter positions there is a direct infiltration from the uterine tumour; in the former this may be absent.

Adenoma of the ovary.—A pure adenoma of the ovary, occurring as a solid tumour composed of epithelium-lined tubules, is very rare; but, on the other hand, the cystic adenoma, more commonly known as the **multilocular ovarian cyst**, is of very frequent occurrence, and may reach a size which is not equalled by any other tumour. The cystic adenoma occurs as a smooth, lobulated tumour composed of a number of cysts held together by fibrous septa. On section it is often found that the bulk of the tumour is composed of a single cyst, in connexion with which there are numerous others of smaller size and often fibrous areas in which minute cysts can just be recognized with the naked eye or seen with the microscope. Occasionally, by the breaking down of the septa between the cysts, the whole tumour is converted into a unilocular cyst. Except in the earlier stages of its development the ovary itself cannot be recognized in a cystic adenoma.

Two varieties of multilocular ovarian cyst are usually recognized —the simple and the papillomatous In the *simple* variety the cysts contain a mucoid fluid, colourless or stained brown with blood pigment. In the larger cysts the fluid becomes more serous. It is among tumours of this variety that the enormous dimensions mentioned above may be reached. In the *papillomatous* form the cysts usually contain serous fluid, and the intracystic growths may take the form of small, scattered, villous tufts, or larger, cauliflower-like masses, which may completely occupy the cysts. Occasionally the papillomatous growths may project through the ruptured wall of a cyst and continue to grow on its surface. In rare instances the cells detached from a ruptured ovarian cyst may, by implantation, give rise to multiple papillary growths on the peritoneum, which are, however, of little practical significance.

A much more important result has been observed to follow the rupture of a mucinous cyst into the peritoneum. The mucin-secreting cells become implanted on various parts of the peritoneum and give rise to the accumulation of enormous masses of mucinous material. This condition, first described by Wirth in 1884, has received the

name *pseudo-myxoma peritonei*. Although it cannot be dealt with radically by operation, relief may be afforded by the periodical removal of the masses of mucinous growth.

It is an important fact that in a small percentage of cases of papillomatous ovarian cyst the disease pursues a malignant course,



Fig. 96.—Microscopic section of cystic adenoma of ovary.

although the tumour may not, to the naked eye, differ from a simple tumour.

Examined microscopically, the cysts of a simple mucinous cystic adenoma are found to be lined with a single layer of columnar epithelial cells, the free extremities of which are distended with mucin (Fig. 96). In the fibrous tissue surrounding the cysts are seen in places tubules, lined with columnar or cubical cells, which have originated by outgrowths from the cysts themselves. In the papillomatous form the intracystic growths are covered with a cubical or

columnar epithelium. The origin of the ovarian cystic adenoma has been very variously interpreted, but the view most generally accepted at the present time is that the tumour arises in collections of cells of the germinal epithelium which have suffered arrest of development.



Fig. 97.—Sebaceous adenoma of labium majus, in section. *Nat. size.*

(From a case under the care of Herbert Spencer.)

Adenoma of the sebaceous glands. —It has already been pointed out that the name adenoma has been incorrectly applied to certain chronic inflammatory affections of the skin in which a hyperplasia of the sebaceous glands is a marked feature. True sebaceous adenomas are undoubtedly rare, unless the view held by Bland-Sutton and some other pathologists is accepted, that certain tumours of the skin which clinically resemble sebaceous cysts are in reality sebaceous adenomas, and consist of newly formed glands rather than of a gland merely enlarged by distension The tumour which is shown in the accompanying illustration (Fig. 97) seems to be an undoubted example of a simple glandular tumour of the sebaceous

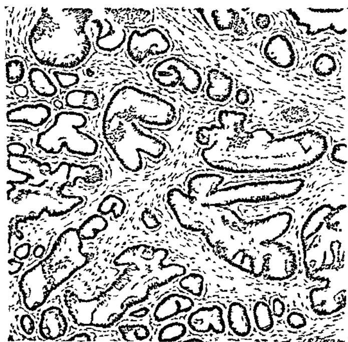


Fig. 98.—Microscopic section of the sebaceous adenoma illustrated in Fig. 97.

type. It was situated beneath the skin of the inner aspect of the labium majus, and measured 2·5 cm. in its longest diameter. Microscopically, the tumour is seen to be a racemose adenoma, and in some of the larger spaces papillary growths project into the lumen (Fig. 98).

It has been suggested that some of the small calcareous tumours occasionally found beneath the skin, and formerly described as osteomas, arise in sebaceous adenomas. It is interesting, however, to note that Shattock has shown that in these tumours the calcification may be associated with a very pronounced horny change in the epithelial cells of the tumour, and he suggests that such tumours may arise in connexion with the hair-follicles and not in sebaceous glands.

PAPILLOMA

A papilloma is a simple tumour which, in its structure, corresponds more or less closely with the papillæ that are normally present in the skin and some mucous membranes. A papilla consists of a connective-tissue outgrowth, containing looping blood- and lymph-vessels, and covered with epithelium of the stratified or columnar type. In a papilloma the component papillæ attain a size much greater than the normal, and are often compound, secondary papillæ springing from the primary ones. In this way the tumour may assume a large size and a most complex structure, the papillæ sometimes taking the form of delicate branching villous processes, and at other times being fewer in number and club-shaped, so that the tumour presents a cauliflower-like appearance. In other tumours, especially those covered with stratified epithelium, the intervals between adjacent papillæ are so completely occupied by the proliferated epithelium that the villous character of the surface is lost, and the tumour is merely velvety, warty, or nearly smooth. Papillomas may be sessile or pedunculated, and sometimes the pedicle of even a large tumour is very slender.

In considering tumours of papillary structure, it is necessary to point out the extreme difficulty of drawing a sharp line of distinction between the true papillomas and certain papillary hyperplasias resulting from chronic inflammation of the skin and those mucous surfaces in which papillæ are normally present, and it may be well to give a few illustrative instances.

As the result of the irritation of gonorrhœal and other discharges, extensive papillomatous formations are not uncommon on and around the external genitalia (venereal warts).

In certain forms of chronic inflammation of the mucous membrane

of the tongue the formation of localized warty growths is a not uncommon manifestation.

Tuberculosis of the skin and mucous membranes frequently assumes a form in which the papillary character is so marked as closely to simulate a tumour. This is particularly striking in the form of tuberculosis of the skin known as lupus verrucosus, as well as in some forms of tuberculous disease of the intestines, especially the cæcum and rectum, where the resemblance to a tumour may be very close.

Other instances of the formation of papillomatous growths as the result of direct local irritation are afforded by cases in which villous outgrowths of the mucous membrane of the gall-bladder or of the pelvis of the kidney have been found in association with calculi. Papillary growths in the rectum and bladder may similarly be caused by the *Schistosoma hæmatobium* (*Bilharzia hæmatobia*). Such illustrations, which might readily be multiplied, are sufficient to show that papillomatous growths are frequently the direct result of chronic irritation.

In some respects papillomas, especially of mucous membranes, have a close affinity with the adenomas. The same tissue elements exist in both tumours, but in different relations, for whereas in the adenoma the epithelium forms a lining to spaces in the stroma, in the papilloma the epithelium covers the surface of the connective-tissue projections. A transitional condition is presented by certain tumours in which the surface has a typical papillomatous structure, whilst in the deeper parts of the tumour epithelium-lined spaces are present. A tumour of this mixed structure is well illustrated by certain simple tumours of the rectum

Another matter of great practical importance, and often of considerable difficulty, is the distinction between simple papillomas and certain malignant growths with a villous or warty surface. The difficulty is chiefly met with in certain papillary carcinomas of mucous membranes, as, for instance, of the mouth and bladder. The tumour in such cases is necessarily sessile, and the surface is rarely so distinctly or regularly papillary as in a simple tumour, but the essential difference is in the character of the base. The papilloma is entirely an outgrowth from the surface. whereas in the malignant growth, in addition to the outgrowth from the surface, there is a downward extension into the deeper tissues This can often be recognized by careful investigation of the base of the growth, but in all cases microscopic examination should be undertaken.

Papilloma of the skin.—Many forms of papillary hypertrophy affecting the skin are rather of the nature of an inflammatory overgrowth than a true tumour. Thus the *simple warts* which are common, especially on the hands, in children, are very probably infec-

tive. They often develop rapidly and may as rapidly disappear, and not uncommonly affect several members of the same family. They consist of a *group* of *slender elongated papillæ* covered with thickened, horny epithelium. A *corn* results from prolonged intermittent pressure on the skin, and, except in moist situations, is characterized by the formation of a hard, conical, horny thickening. Immediately beneath this the papillæ atrophy, but around it they may show a slight degree of hypertrophy. In the tissues beneath a corn a small adventitious bursa may be present, and is liable to be the seat of



Fig. 99.—Microscopic section of a venereal wart.

suppuration, which in feeble elderly subjects may lead to serious results.

Undoubtedly the most striking papillomatous growths of the skin are the *venereal warts* to which reference has already been made. (Fig. 99.) They occur in their most exaggerated form in the female, on the external genitalia and around the anus, *where they may reach a large size*, spreading over considerable areas, and having a cauliflower-like form The sodden masses of epithelium which cover the papillary *processes cause by their decomposition a peculiarly offensive discharge.* It is necessary to distinguish clearly between the venereal papillomas and the condylomas, or "mucous tubercles," which occur in similar

situations in the secondary stages of syphilis. Condylomas merely represent a modified form of a squamous syphilide due to its situation in a part which is persistently moist, so that, instead of the scaly patch that characterizes the eruption elsewhere, the thickened epithelium accumulates in soft masses over the enlarged papillæ. The mucous tubercle never assumes the typically papillomatous form of the venereal wart nor the large size often attained by the latter.

True papilloma of the skin is undoubtedly rare, but is occasionally met with, especially on the face, as a small tumour composed of a tuft



Fig. 100.—Microscopic section of a papilloma of skin of face.

of slender, elongated papillæ (Fig 100). By the heaping up of the horny epidermic covering of a papilloma one form of *cutaneous horn* may be produced. In rare instances such a horny outgrowth has attained a large size, producing a striking deformity In the base of the horn is the vascular papillary projection on which it originated Reference will subsequently be made to cutaneous horns which occasionally form from sebaceous cysts (p. 626).

In this place it will be convenient to refer to certain formations which occur in the skin, but of which the papillomatous structure is not always a salient feature We refer to *soft warts* and *congenital moles*. The soft wart occurs as an isolated tumour, the surface of which is in some instances papillary, but often smooth, or at the most

marked by shallow clefts; the tumour may be pigmented. The congenital mole may present itself as a simple pigmented area in the skin, or as a raised warty patch, often hairy and deeply pigmented. Such hairy, pigmented moles may involve large areas, and, if present on the face, occasion hideous disfigurement.

The pigment in these different forms of simple melanoma is present in spindle-shaped or stellate cells in the corium (chromatophores), and also in the deeper layers of the epidermis. Some observers believe that processes of the chromatophores may extend between the epithelial cells.

In the soft wart, and also in the congenital mole, there are sometimes found beneath the epidermis certain cell masses (nævus cells), the origin and nature of which have been the subject of much discussion. The nævus cells are in some cases small and round or oval, but in other specimens they are larger, richly protoplasmic, possess a round nucleus, and are more epithelioid in character.

According to the original view of von Recklinghausen, these nævus cells are endothelial in nature, and the name lymphangio-fibroma was applied to such growths. Ribbert believes them to represent an early stage in the development of the chromatophores, before pigment has formed in the cells. Unna, on the other hand, claims to have traced the nævus cells in the fœtus from the Malpighian layer, although the continuity is lost. It will thus be seen that opinions differ as to whether the cells in question are of epithelial or connective-tissue origin.

The chief practical importance of these pigmented moles is their liability to be the starting-point of certain pigmented growths. Such tumours must originate in the nævus cells, the chromatophores, or the deeper cells of the epidermis. Their histological structure is that of sarcoma or of endothelioma rather than of carcinoma. On the other hand, the marked tendency to metastases in the lymphatic glands, and their close connexion, in some cases, with changes in the deeper layers of the epidermis, suggest a carcinomatous nature. The latter fact, however, is discounted by the possibility of chromatophores being intercalated among the deeper epithelial cells. We think that the majority of these tumours are sarcomatous or endotheliomatous, and that the origin of any of them from the epithelium has not been proved.

Reference has already been made to the pigmented patches met with in cases of neuro-fibromatosis (p. 406), and it is probable that some pigmented moles are allied to this disease.

Papilloma of mucous membranes.—Papillomas occasionally occur on the mucous membrane of the *mouth*, such as the lips, cheeks, gums, tongue, and palate. A simple pedunculated papilloma in these situations is rare, but may occur in such a situation as the

tip of the uvula. More often in these regions a papilloma assumes the form of a small, sessile, warty growth, whilst on the tongue warty or papillomatous patches may occur as one of the manifestations of chronic superficial glossitis. Such warty growths, especially on the tongue and lips, should always be regarded with grave suspicion, for, even if not already cancerous, the likelihood of the later development of malignant disease is very great. For this reason no hesitation should be felt in urging their free removal without delay.

Papillomas of the *larynx* are more common than any other simple tumour in this part, and are much more frequent in children than in adults. The favourite site is the vocal cords, but when multiple they may grow also on the ventricular bands, laryngeal surface of the epiglottis, and upper part of the trachea. A dangerous degree of destruction may result.

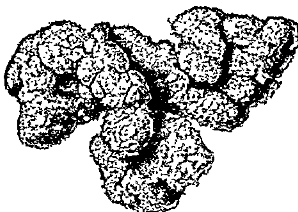


Fig. 101.—Papilloma of rectum. The tumour is very lobulated and the surface composed of delicate villous processes.

Papilloma of the *intestine* is rare, except in the rectum. In several recorded cases multiple papillomas of the intestine have occasioned hæmorrhage from the bowel. In the *rectum* (Fig. 101) a papilloma may reach a large size, forming a tumour which resembles the flower of a chrysanthemum; and although at first the growth is probably always sessile, it tends gradually to become more and more pedunculated, so that eventually it may be extruded from the anus during the expulsive efforts of the bowel. Papilloma of the rectum is more common in women than in men. The papillæ composing the tumour are covered with *columnar epithelial cells*, amongst which goblet cells are often present, and the central part of the tumour may present a structure resembling that of an adenoma.

Papilloma may occur on the mucous membrane of any part of the *urinary tract*—calyces and pelvis of the kidney, ureter, and bladder. In the *bladder*, papilloma is the most common simple tumour, and, as elsewhere, may be single or multiple. When single, the tumour is usually pedunculated, and its favourite site is the neighbourhood

of the ureteric orifices (Fig. 102). When multiple, the tumours are usually sessile and form small tufts, which in some cases are thickly scattered over all parts of the bladder wall. The delicate structure of these villous tumours and their vascularity explain the hæmorrhage which so readily occurs from them, especially when they are

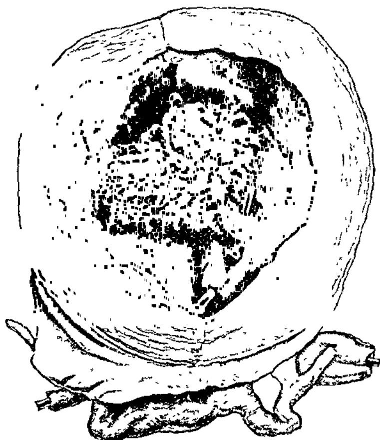


Fig. 102.—Papilloma of urinary bladder. The pedicle of the tumour is attached near the orifice of the left ureter.

(*This and the preceding figure are from specimens in University College Hospital Museum.*)

squeezed by the contracting bladder wall. Apart from their recognition by cystoscopic examination, small fragments of the villous processes of the tumours can sometimes be demonstrated with the microscope in the urine.

Similar villous tumours occurring in the *pelvis of the kidney* are an occasional cause of renal hæmaturia, and the rare association of such tumours with renal calculi has already been mentioned. In some recorded instances papillary growths have been found in the kidney,

ureter, and bladder simultaneously, the tumours in the bladder being sometimes limited to the neighbourhood of the orifice of the affected ureter. In such cases the conclusion seems probable that the growths have spread along the urinary tract by a process of simple transplantation.

The epithelium covering the papillomas of the urinary tract is of the transitional stratified form which is normal to the part.

In a case recently in University College Hospital, hæmaturia due to a papilloma of the bladder occurred eight years after the removal of the left kidney for a villous carcinoma. In this connexion it may be pointed out that it is extremely difficult, if not impossible, to determine whether a papillary tumour of the urinary tract is entirely benign.

Intracystic papilloma.—In addition to the papillomas arising from cutaneous or mucous surfaces, others not uncommonly arise from the inner surface of various forms of epithelium-lined cysts, such as those occurring in the breast and ovary.

In the *breast*, such intracystic papillomas may be single or multiple. The isolated form is usually found in a cyst formed by dilatation of one of the large ducts—*duct papilloma*. The tumour may have a delicate villous structure, being composed of branching vascular papillæ, and may partially or completely fill the cyst in which it grows. In the latter case the closely packed processes of the tumour may so completely fill and distend the cyst that the cyst wall assumes the appearance of a thin, fibrous capsule surrounding the tumour. It frequently happens that the cyst still retains its communication with the duct from which it originated, and thus a discharge, often bloodstained, occurs from the nipple, just as in a vascular papilloma of the bladder or rectum hæmorrhage is a prominent symptom.

Besides the duct papilloma, which presents itself as an isolated tumour of the mamma, multiple intracystic papillary growths are sometimes met with in connexion with the cystic degeneration which may affect one or both breasts. In this disease a part or the whole of the gland is transformed into a number of cysts varying in size, and often containing papillary ingrowths similar in character to the single form above described.

It is very important to recognize the essential difference between simple papillomas and that form of columnar carcinoma which, originating in the larger ducts, assumes a villous form (p. 608). In the latter tumour intracystic papillomatous growths may be present, but a careful histological examination will reveal the important fact that the epithelial growth is not confined to the interior of a cyst, but extends also into the tissues outside and beyond the cyst wall.

Although the villous form of columnar-celled carcinoma of the *breast* is probably of comparatively low malignancy, it is very likely that this feature has been exaggerated by the inclusion among the villous cancers of certain papillomas of a benign nature.

In the *ovary*, intracystic papillomas are common in one variety of multilocular cyst, and have already been mentioned in speaking of that disease (p. 473). In many respects they closely resemble the intracystic papillomas of the breast, and it is a matter of great practical importance that in some cases an ovarian tumour, indistinguishable from a simple papillomatous ovarian cyst, may pursue a malignant course, recurring locally after removal, and ultimately proving fatal.

Papillomas also occur in parovarian cysts. Occasionally masses of papillomatous growth are found on the surface of the ovary independently of any cystic disease, and may form a tumour of considerable size. Such growths are entirely benign, and show no tendency to implantation.

MALIGNANT TUMOURS

It has already been pointed out that a malignant tumour differs from a simple or benign tumour in its mode of growth; that in whatever part it originates it exhibits an invariable tendency to invade and destroy the surrounding tissues, and often, sooner or later, to disseminate itself in distant parts. It has further been stated that in its structure a malignant tumour is usually strikingly "atypical," deviating widely from the structure of the part in which it originated, and that the cells composing it become endowed with a power of progressive growth which continues until a fatal result is almost invariably produced. Tumours exhibiting malignant characters are represented by two great classes—the *sarcomas* or malignant non-epithelial tumours, and the *carcinomas*, or malignant epithelial tumours. Some degree of confusion still exists in the nomenclature of malignant growths on account of the popular use of the name "cancer" for all tumours of this nature—a relic of the times when sarcoma and carcinoma were imperfectly recognized as distinct forms of growth. The older writers, depending mainly for their descriptions of tumours upon some very obvious feature, such as consistence, adopted the terms "encephaloid" and "scirrhus" for those presenting marked softness or hardness respectively. Again, it is still very usual to apply the name "epithelioma" to those forms of carcinoma which originate from a surface epithelium. Thus, although

known as a car-

In order to simplify the nomenclature, and also because the name "epithelioma" has been applied, especially by French pathologists, to certain epithelial growths of a simple nature, only the term "carcinoma" will be used in this article for all forms of malignant epithelial growth.

Distinctive characters of carcinoma and sarcoma.—Before proceeding to describe the different forms of malignant tumours it will be convenient to consider certain features common to all, and it will render this easier if the essential characters of the sarcomas and carcinomas respectively are first described.

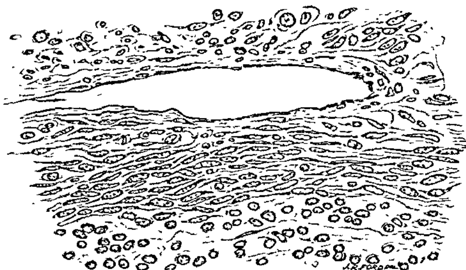


Fig. 103.—Microscopic section of spindle-cell sarcoma, showing a blood-space, the endothelium of which lies in contact with the tumour cells.

The essential constituent of each form of malignant tumour is represented by the *cell elements*, although, especially in the carcinomas, the characters of the stroma will need subsequent consideration. A sarcoma consists essentially of a mass of more or less undifferentiated connective-tissue or mesodermal cells, whilst a carcinoma is composed essentially of epithelium, which, whilst growing in an irregular manner, usually preserves recognizable resemblance to the squamous, columnar, or spheroidal varieties of epithelium in which the tumour had its origin.

It is true that sometimes it is difficult to distinguish definitely, on cell characteristics alone, between some forms of spheroidal-cell carcinomas and some round-cell sarcomas, and in these cases certain other features of the tumours must be utilized to help in the diagnosis. It may be said generally that in carcinomas the epithelial

cells still exhibit the feature that they lie in immediate contact one with another, or at the most are separated by a very small amount of intercellular substance. The *cell masses* are, however, usually *sharply defined from the stroma of the tumour or the tissues into which they are extending*. This is especially seen in sections which have been treated with various hardening reagents, and in which a *distinct interval often* separates the cell mass from the tissue around it. In the ordinary round-cell sarcoma, on the other hand, the cells are less regularly arranged, and may be separated by a definite amount of *homogeneous ground substance*, or even by a fine reticulum.

The relation of the blood-vessels to the tumour cells is a matter of great importance. In a sarcoma the blood-vessels are usually very numerous, and extend actually into the cell masses among the cells themselves (Fig. 103). The vessels, moreover, are devoid of proper vessel walls, and frequently consist merely of clefts or spaces among the cells bounded only by specially arranged cells, often in the form of short spindles lying end to end (Fig. 103). The arrangement thus suggests the appearances seen in the normal process of the development of connective tissue. In a carcinoma, on the other hand, the small blood-vessels, *although they may be very numerous, are confined to the tissues intervening between the cell masses*, and do not extend into the latter; they present the appearance of ordinary arterioles, venules, and capillaries.

The relation of the tumour cells of malignant growths to the *lymphatics* is *also of great practical importance*, although no definite differentiation between the two classes can be based upon it. The evidence of lymphatic invasion and dissemination in carcinoma is usually very obvious at the spreading margin, where the tumour cells can frequently be seen lying in slender columns in the lymph spaces, and often surrounded by the flattened endothelial *cells of the latter* (Fig. 104). Although the statement will require some qualification, it may be laid down as a general rule that in the sarcomas dissemination takes place chiefly by way of the blood-vessels, whilst the carcinomas extend mainly along the lymph-channels. For example, in the case of a sarcoma of the periosteum of the tibia we should look for evidences of secondary deposits especially in the lungs, whilst in the case of a carcinoma of the skin of the leg the first evidence of dissemination is likely to be found in the lymphatic glands of the groin.

Attempts to discover any histological feature by which the cells of malignant growths can be *distinguished from those of simple tumours* and other pathological conditions have not hitherto been successful.

Evidence of malignancy.—The malignancy of a tumour may be manifested locally and generally—*locally* by its destructive action

upon the tissues in which it arises and those directly continuous with them, and *generally* by its power of dissemination, with the production of secondary deposits or "metastases" in distant parts. Different tumours manifest these evidences of malignancy in very varying degrees, so that, whilst in some instances the malignancy of a growth is shown more or less exclusively by its destructive action on

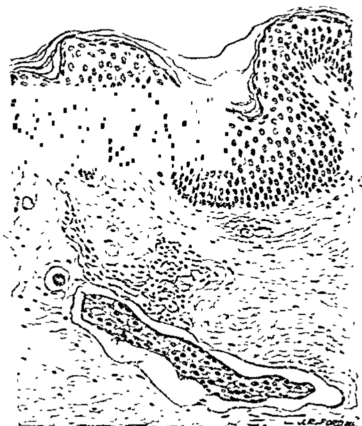


Fig. 104.—Microscopic section of skin, showing a column of carcinoma cells in a lymphatic. The primary growth was situated in the breast.

the tissues surrounding it, in other cases the tumour, although producing but little local damage, manifests its malignancy by an early and often widely spread dissemination in distant parts.

To the naked eye the outline of a malignant growth is in section often quite defined, but, unlike the simple tumours, this apparent margin of the growth does not represent its actual limits, for around it is a more or less extensive zone in which careful microscopic examina-

tion shows that the tumour cells are invading the surrounding tissue; and in planning an operation for the removal of a malignant tumour it is essential that the tissues in which this local extension is likely to be taking place should be freely removed. The evidence strongly supports the view that every malignant growth is local in its origin, and that recurrence after operation means that the operation has failed to remove completely the tissues which have already been invaded. The extirpation of a simple growth requires only the complete removal of the tumour itself, whilst the thorough extirpation of a malignant growth necessitates an operation the magnitude of which may seem to be out of all proportion to the macroscopic extent of the disease. It is worthy of notice that an undoubtedly malignant growth, and especially some varieties of sarcoma, may exhibit a well-marked tendency to encapsulation, whilst it is actually infiltrating the surrounding tissues. Thus, in certain sarcomas of the tonsil such a condition has been observed even when the presence of muscular tissue inside the capsule gives clear proof of the malignant nature of the growth.

In studying the behaviour of a malignant growth at its advancing edge, it is most important to observe the part played by the blood- and lymph-vessels, for it is clearly by these routes that dissemination must be brought about. The mode of invasion of the blood-vessels by the tumour cells and the behaviour of the latter in the interior of the vessels have been studied particularly by Goldmann of Freiburg, and Schmidt of Jena. Goldmann, by using a special stain for the elastic tissue in the walls of the small arteries and veins, showed that these vessels are invaded by the cells of the growth in the peripheral zone, the invasion of the vessel walls taking place by way of the vasa vasorum, and that whilst in the arteries the tumour cells rarely proceed farther than the outer coat, in the veins they are generally found beneath the intima. From these and other observations it appears certain that even in the early stages of malignant disease the tumour cells must find their way into the general circulation, and that if every such cell became the starting-point of a secondary deposit, extensive metastases in the lungs would be an almost universal occurrence. There is, however, good reason for believing that in some way the cells are often destroyed in the circulation and fail to develop into metastases. In this connexion the work of Schmidt is of great importance. Among 41 cases of carcinoma which he examined systematically to determine the modes of dissemination were 15 cases of abdominal carcinoma in which cancerous emboli were present in the small arteries of the lungs, often without any macroscopic signs of secondary deposits. In one case, however, the affected arterioles could be seen as fine white rami-

fications. In the youngest emboli the cancer cells, without stroma, were surrounded by blood-corpuscles, but showed mitoses, and were

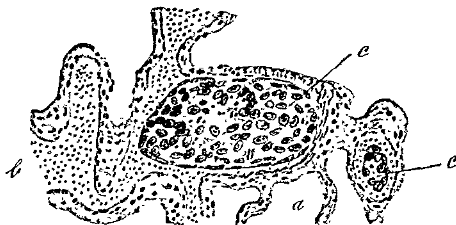


Fig. 105.—Emboli of carcinoma cells in a branch of the pulmonary artery (*c*, *c*). *a*, Pulmonary alveolus; *b*, blood.

evidently capable of proliferation (Fig. 105). In many emboli, however, the cancer cells were surrounded by a thrombus (Fig. 106), and

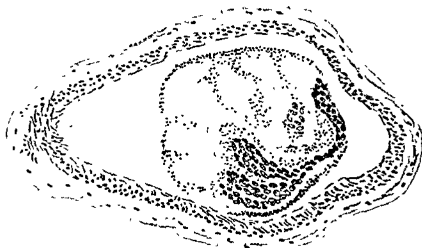


Fig. 106.—Embolus of carcinoma cells surrounded by a thrombus, in a branch of the pulmonary artery.

as the result of organization of the thrombus, which was demonstrated in all the cases but one, the cancer cells gradually underwent

retrogressive changes (Fig. 107). First, the protoplasm disappeared, only the nuclei remaining, and finally a completely organized thrombus was left in which no traces of the cancer cells could be seen. Schmidt further states that the cancer cells in the arteries of the lungs may extend continuously along the lumen into the capillaries and veins without invading the vessel walls. This occurred in 9 of the 15 cases, and serves as an explanation of the presence of metastases in the systemic circulation without their presence in the lungs.

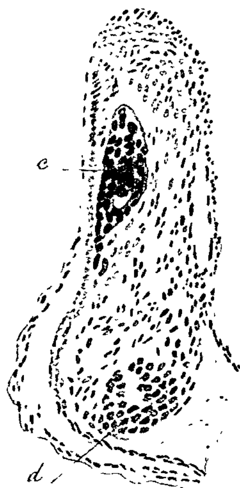


Fig. 107.—Embolus of carcinoma cells surrounded by organized tissue in a branch of the pulmonary artery. At *c* the carcinoma cells are intact; at *d* they are undergoing degenerative changes.

(This and the two preceding figures are after M. B. Schmidt, "Die Verbreitungswege der Karzinome.")

Although such observations show that emboli of the cells of malignant tumours do not necessarily develop into secondary growths, it is still certain that direct invasion of the vascular system is an important route by which dissemination (Fig. 108) takes place. A special instance of the same process is frequently observed in cases of malignant disease occurring within the area drained by the portal vein, and thus in abdominal carcinoma it is very common to find the liver, with perhaps the lymphatic glands corresponding to the site of the primary growth, to be the only seat of secondary deposits.

It has already been pointed out that in the zone of infiltration around a malignant growth, especially the carcinomas, the tumour cells can be demonstrated in the lymph-vessels, by means of which they readily reach the nearest set of lymphatic glands and occasion the enlargement which is so frequently the first evidence of metastasis. In the early stages the invasion of a lymphatic gland is usually evidenced by the presence of tumour cells

and cell masses in the sinuses of the cortex, but later the disease spreads to the medullary portion, and eventually the gland is replaced by a uniform mass of growth. From the gland first affected the disease tends to spread until many adjacent sets become involved.

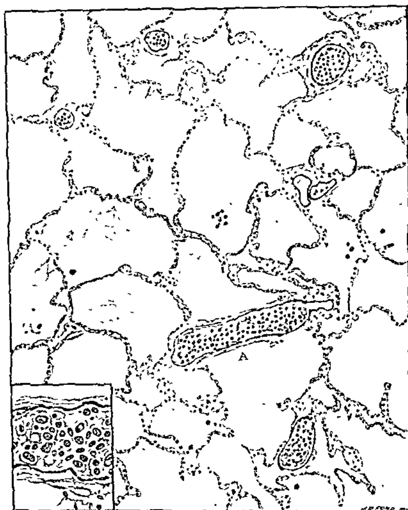


Fig. 108.—Microscopic section of lung showing intravascular metastases of carcinoma. Inset, enlarged view of section at A.

In dealing with the dissemination of malignant disease by the lymphatic system, it is necessary to refer to the important part played by the thoracic duct. Since Weigert reported a case in which the duct was completely blocked by a deposit of carcinoma secondary

to a growth in the rectum, many cases have been recorded in which a similar condition was present, or in which a secondary deposit of growth in the lymphatic glands above the left clavicle has been associated with deposits of growth in the duct.

Sampson Handley has advanced the view that many of the phenomena of metastasis usually assigned to dissemination by way of the blood-stream are in reality due to extension along lymphatic vessels. According to him, the tumour cells are not carried merely in the direction of the lymph-stream, but spread in ever-increasing circles by active growth along the lymphatic vessels (lymphatic permeation) from the primary tumour. In this way it is supposed that even distant parts may be reached and secondary deposits produced, while the direct connexion of the latter with the primary growth is interrupted by the degeneration of the cancerous lymphatics as the result of an inflammatory fibrosis which occurs around them. Handley has applied this theory of direct lymphatic permeation to explain some of the phenomena of abdominal metastasis in cases of mammary carcinoma, and supposes that the invasion of the abdominal cavity occurs by way of the communication of the parietal and abdominal lymphatics, especially in the region of the epigastrium Having once reached the peritoneal cavity, the further extension of the disease, it is supposed, may be dependent upon a simple process of transplantation of the cancer cells on the serous membrane and their subsequent growth into the subjacent viscera—as, for instance, the ovaries. Whilst fully recognizing the value of Handley's work, we cannot entirely accept his conclusions regarding the part played by the lymphatic and circulatory systems respectively in the dissemination of malignant disease, and find it difficult to believe that, for instance, the metastases of mammary carcinoma in the bones occur by way of the lymphatics. Not only is it doubtful whether lymphatics exist in the medulla of bone, but it has been shown by Piney that metastases in the bone-marrow are, in their earliest stages, located within blood-vessels.

A primary malignant growth is usually single, but a considerable number of cases are on record in which two or more such tumours have occurred in the same individual and, being instances of different forms of growth, cannot be regarded as secondary one to another. Thus, among numerous cases of this kind recorded by Beadles is one of spheroidal-cell carcinoma of the breast and squamous-cell carcinoma of the cervix uteri, and another of carcinoma of the breast and sarcoma of the skin of the groin. Gotting also has placed on record the case of a man, aged 58, who had carcinoma of the larynx with secondary growths in the lymphatic glands, carcinoma of the pylorus, and carcinoma of the rectum. Such exceptional cases do not invalidate the general rule that a primary malignant tumour is usually solitary.

Causation of malignant tumours.—Already, in speaking of the nature and causation of tumours in general, reference has been made to some of the views which have been held concerning the origin of malignant as well as benign growths. For instance, it has been pointed out that, according to some authorities, tumours originate, not in the ordinary cells of the tissues, but in cells of an embryonic type, which remain among the ordinary tissues, ready under the influence of some unknown cause to take on the independent growth which results in the formation of a tumour. The problem of the cause of malignant tumours may, indeed, be presented by the question—What occasions the abnormal proliferation of connective-tissue cells by which they become a sarcoma, or of epithelial cells which constitutes the growth of a carcinoma? In a more concrete form the question presents itself thus—Is the growth of a malignant tumour caused by a specific infective agent entering the body from without, or by some permanent modification of the metabolic processes of the cells?

On general grounds several difficulties present themselves in accepting the view that malignant growths are infective in nature and caused by a microbic agent. In undoubtedly infective diseases, such as tuberculosis, the extension of the disease occurs in inverse proportion to the vitality of the tissues, whereas in the case of malignant tumours it is proverbial that the growth is most rapid in the young and vigorous, and correspondingly slow in aged subjects with tissues of lowered vitality. Again, it may be argued that if malignant growths were due to a microbic agent their spontaneous arrest and involution would not be very uncommon, whereas such an occurrence, as will [illegible] rarity.

The [illegible] he metastases of carcinoma [illegible] growths almost always correspo[illegible] primary growth, and the coexistence of carcinomas of different structure is extremely rare. If the cells of a carcinoma contain a living parasitic agent, upon which the cell proliferation depends, it might be supposed that this infective body, carried to parts in which epithelium of another type exists, would cause the development of a corresponding form of carcinoma, or—to give an example of what might be expected, but as a matter of fact does not occur—a spheroidal-cell carcinoma of the breast involving the skin would be likely to infect the squamous epithelium of the latter and cause the growth of a squamous-cell carcinoma.

In the search for parasitic bodies in the cells of malignant tumours the carcinomas have chiefly been the subject of investigation, and observers too numerous to mention have described and figured cancer

cells in which bodies believed to be parasites were present. The value of this work is very great when regarded merely as observations of histological appearances in cancer cells, but the interpretation of the facts observed has led to much discussion, the outcome of which is that the bodies are for the most part not regarded as parasitic, but can be explained as the various forms of cell degeneration, endogenous cell division, cell inclusions, or irregular forms of mitosis. Organisms described by some observers and capable of cultivation in artificial media have not so far been proved to have any causal significance in the production of the malignant growths in which they were found.

Closely related to the question of the nature and causation of malignant growths is the subject of their **communicability** from one individual to another. Evidence of this may be sought for experimentally in the lower animals or, as the result of accident, in the human subject. In view of the great frequency of the disease, it is remarkable how very few cases are on record which appear to illustrate its transmission from one individual to another. Such an occurrence might naturally be expected to occur, if at all, in cases of superficial disease, and especially in ulcerated carcinomas of the skin and mucous membranes. Among the recorded cases are a few in which carcinoma appears to have been transmitted by coitus from the genitalia of one sex to those of the other, and among other examples may be mentioned a few instances in which a surgeon has been believed to become inoculated during an operation on a cancerous patient. The accidental communication of the disease from man to the lower animals, and vice versa, has also been reported.

The experimental transmission of malignant growths in the lower animals has been the subject of much investigation both in this country and abroad. Hanau, in 1889, and Moreau, in 1894, made successful transplantations of malignant growths. The former transplanted a carcinoma of the vulva from rat to rat, and the latter a mammary carcinoma from mouse to mouse. Jensen and Borel followed up these observations with an exact investigation of the process of transplantation; and subsequent workers, especially in connexion with the Imperial Cancer Research Fund, have added to our knowledge. Thus, among other important observations, it has been shown that of the two elements of a cancerous graft—the stroma and the epithelium—the former degenerates, the epithelium alone constituting the essential part of the growth, whilst a new stroma is developed as the result of a reaction in the surrounding tissues. It has also been shown that the primary transplantation of a carcinoma is more difficult to effect than subsequent transplantations, and from this it has been concluded by Bashford, Murray, and Haaland

that the epithelial cells of the growth become modified by a process of adaptation in successive transplantations. Of especial interest is an observation of Ehrlich and Apolant, that in a certain number of cases a transplanted mouse-carcinoma may give rise to sarcoma in conjunction with the epithelial growth—the first evidence of the experimental production of a malignant growth *de novo*. Murray states that the sarcomatous elements in such circumstances are derived from the host.

The subject of the production of **immunity** to the growth of malignant tumours in animals has engaged the attention of many workers. In 1901–3 Jensen recorded the complete disappearance of tumours from mice which had been successfully inoculated with carcinoma, and suggested that this was due to natural refractoriness of the tissues of the inoculated animals, and possibly also to a resistance produced by absorption of the inoculated material. Following up this line of investigation, much experimental work has been done with a view to testing the value of inoculation in inducing immunity, but the work of Haaland has shown that, in a mouse with spontaneous cancer, inoculation with the growth from another animal does not prevent successful grafting of the spontaneous tumour or the formation of metastases A study of the action of X-rays in animals appears to show that small doses may increase their resistance to successful inoculation.

Allied to the question of the communicability of carcinomatous and other malignant growths is that of their **auto-inoculability.** The evidence on this subject was carefully discussed by Butlin in the Bradshaw Lecture delivered before the Royal College of Surgeons in 1905. Butlin showed how very few of the cases supposed to illustrate the possibility of the inoculation of cancer from one part of the body to another by mere contact will bear full investigation. The evidence, however, seems conclusive that such an event does occasionally occur. Among the most striking examples are those showing the spread of cancer from one side of the vulva to the other, the growths being on parts which are naturally in contact, but the two growths having no direct continuity across the middle line. Similarly, Newman of Glasgow has recorded a case in which a squamous carcinoma of the left false vocal cord was followed by the development of a similar ulcer on the right cord. The nature of each growth was confirmed by microscopic examination, and there was no continuity between them either in front or behind. In the lips Butlin was able to find only one instance of auto-inoculation of which the truth seemed beyond dispute. The case, recorded by von Bergmann, was that of a man who had a cancer of the middle of the lower lip, and exactly opposite to it on the upper lip was a similar growth. Both growths were

removed and their nature was confirmed by microscopic examination. Macewen communicated to Butlin the following extraordinary case: A man with an ulcerated carcinoma of the lower lip had contracted the habit of rubbing the lip and then the tip of the nose with the same finger. Twenty months after the removal of the disease of the lip the patient returned with a large ulcer on the tip of his nose. This also was removed: it presented the same microscopic structure as the ulcer of the lip. In considering this subject it is important to remember that multiple developments of carcinoma are not very uncommon in parts which are the seat of a precancerous condition. and in such cases, for instance, as those apparently illustrating inoculation by contact in the vulva, it is conceivable that both growths sometimes arise independently in a part already predisposed to the disease.

The possibility of auto-inoculation has an obvious bearing on the operations undertaken for malignant disease, and suggests the importance of avoiding contamination of the divided tissues from the surface of an ulcerated growth or from exploratory incisions made into it. In a striking case, recorded by Watson Cheyne, it was necessary to perform a laryngotomy hurriedly with the knife which was being used to excise a sarcoma of the upper jaw. Subsequently the only evidence of recurrence was a nodule of growth in the scar resulting from the laryngotomy.

The outcome of the above considerations concerning the communicability of malignant growths in man and in certain of the lower animals, and the occasional auto-inoculation in the human subject, is merely to show that in favourable circumstances the living cells of the tumour can continue to grow in their new surroundings—a modified instance of the phenomenon of metastasis. No proof is thereby afforded that the disease is infective. Indeed, in our present state of knowledge it must be allowed that the existence of a living parasite in malignant growths has not been proved, and still less has any real success attended the attempts made to cultivate any such parasite outside the body and to reproduce a similar malignant growth by inoculation

Predisposing causes of malignant tumours.—In considering the causation of malignant growths, perhaps the most clearly established fact is the frequent development of the disease in tissues which are already altered by various chronic inflammatory changes, often resulting from long-standing irritation. So close appears to be the connexion in some instances, that certain definite *precancerous conditions* are recognized. It is, indeed, in carcinoma that the relation of the disease to **chronic irritation** is most obvious, and, as might be, expected particularly in those superficial forms of the disease which

affect the skin and mucous membranes. In dealing with the different varieties of carcinoma of the skin, reference will be made from time to time to this subject, and it is only necessary in this place to mention such striking instances as the development of cancer of the skin in chimney-sweeps and in workers with tar and paraffin, its occurrence in the Kashmiris from the irritation of the skin of the abdomen and thighs caused by portable stoves of heated charcoal, and the still more striking occurrence of the disease from the prolonged action of X-rays. In all these instances a dermatitis, usually of long duration, precedes the actual development of the malignant growth. The nature of the irritant evidently varies widely, and may be mechanical, thermal, chemical, or infective; but in some instances the causation is possibly more complex, as in the cancer of the scrotum occurring in chimney-sweeps, in which it is uncertain whether the irritation is mechanical or due to some chemical constituent of the soot, such as arsenic, which it is known can by internal administration occasion a chronic dermatitis upon which carcinoma sometimes supervenes. In the case of squamous carcinoma of the skin it may indeed be said that the disease very rarely arises in a previously normal surface, and its occurrence in ulcers, sinuses, and cicatrices will subsequently be mentioned.

In the mucous membranes many salient illustrations of the effect of chronic irritation are seen, although, partly on account of the greater difficulty of observation, they are less numerous than in the skin. Reference may, however, be made to the supervention of cancer of the tongue upon chronic superficial glossitis, cancer of the stomach upon simple chronic ulceration, and the occasional occurrence of cancer in the gall-bladder, and less frequently in the pelvis of the kidney, in association with calculi

In those forms of carcinoma, chiefly of the undifferentiated type, which originate in the epithelium of glandular organs, the relation of the disease to previous chronic inflammation and prolonged irritation is much less clearly defined, partly, no doubt, as the result of the greater difficulty of observation. Taking carcinoma of the breast as one of the commonest forms of the glandular variety, it seems very probable that in some instances the disease arises in connexion with various epithelial proliferations associated with chronic mastitis, although in the majority of cases there is no clinical or pathological evidence of any precancerous condition.

Carcinoma of the thyroid supervening upon a simple goitre, and of the prostate occurring in a gland already enlarged, are other instances of interest in this connexion, and mention must be made of the fact that a carcinomatous change occasionally occurs in the epithelium of a simple tumour, such as an adenoma, papilloma, or teratoma.

A study of sarcoma shows that the relation of this form of malignant growth to pre-existing pathological tissue change is much less evident than in carcinoma. Whereas carcinoma tends to develop more or less gradually in the middle and later periods of life, and often in already damaged tissues, sarcoma is much more common in the earlier periods of life, and develops usually more rapidly in tissues showing no evidence of previous damage. There seems, however, reason to believe that among the sarcomas simple traumatism sometimes stands in a causal relation to the development of the growth. This connexion has, perhaps, most often been apparent in sarcoma of the bones, and an interesting instance is afforded by the occasional development of such a tumour at the site of a previous fracture (p. 532). It must, of course, be remembered that an injury may attract attention to an already existing but hitherto unrecognized tumour, but in the cases apparently illustrating the causal relation of an injury with a sarcoma the interval has been too long to make such an accidental connexion at all probable

Sarcoma rarely develops in tumours of a benign nature, but reference is elsewhere made to the occasional development of the disease in cases of neuro-fibromatosis (p. 406), and also to the fact that an endothelioma, after a long period of apparently benign growth, may assume the characters of malignancy and become transformed into an endothelial sarcoma (p. 515). Mention may also be made in this connexion of the not infrequent supervention of sarcomatous tumours in the disease first described by Paget and known as osteitis deformans Among 34 fatal cases of this disease collected by Elmslie, death was caused in 12 by malignant growths, of which 9 were primary sarcoma of bone. Two specimens from Paget's cases are preserved in the Museum of St. Bartholomew's Hospital, the sarcoma being in one case in the femur and in the other in the skull. Lawford Knaggs and Grüner have recorded a case in which a sarcoma of the femur supervened upon a peculiar form of osteitis, probably identical with that described by Shattock as non-calcifying osteitis, and by von Recklinghausen as osteitis fibrosa. Elmslie refers to a specimen at St. Bartholomew's in which a sarcoma had developed in the site of an old tuberculous affection of the knee. Such cases illustrate the fact that, although in a much less marked degree than carcinoma, sarcoma occasionally arises in tissues which are already affected by some non-malignant pathological change.

If malignant growths are in any sense dependent upon heredity, it is the predisposition of the tissues to the development of the disease, and not the disease itself, which is transmitted. Although the theory of the hereditary nature of cancer has been widely accepted, and striking instances of its occurrence in several members of the same

rise occurs, after which the curve rises with a sudden and steep ascent to the maximum at about 55, whilst in advanced years there is again a rapid fall.

The average age at which carcinoma is most common varies somewhat with the different forms of the disease. Thus, it is somewhat earlier in the stomach than in the rectum, in the tongue than in the lips, and in the uterus than in the breast.

Many instances, properly authenticated, of the occurrence of carcinoma in early life have been recorded. In a paper dealing with this subject, by Philip of Zwickau, the most noticeable published cases have been collected. Among them are the following: Bethe's case of cancer of the rectum in a boy of 10, with secondary growths in the lymphatic glands, liver, and mediastinum; Norman Moore's case of carcinoma of the stomach in a girl of 13; Kühn's case of cancer of the pancreas in a child of 2, with a secondary growth in the lung; and Braunsta's case of squamous carcinoma of a burn scar on the forearm of a girl of 12. As far as we know, the earliest recorded case of carcinoma of the uterus is that by Ganghofner, in which the disease began at the age of 8 years; of the breast, Henry's case, in which the patient was 21 years old.

Bashford has very rightly insisted that in considering the age-incidence of cancer it is necessary to distinguish between the origin of the disease and its growth. Although carcinoma rarely begins in early life, yet in such cases the disease usually exhibits an extreme degree of malignancy and rapidity of growth, and in the same way young animals receive the disease by experimental transference more easily than old ones. The tissues of a young subject are not prone to develop cancer, but are particularly favourable to its growth should it occur. The fact that cancer so rarely arises in early life may possibly be explained on the assumption that it is only in the middle and later periods of life that the requisite longstanding irritation of the tissues has had time to take effect.

In considering the relative **liability of the two sexes** to malignant disease it may be stated that it is more common in women than in men, because of the great liability of the uterus and female breast to carcinoma; but, excluding these parts, the disease is more common in men than in women. Thus the Annual Report of the Registrar-General for 1919 shows that the deaths ascribed to malignant disease numbered 42,144, of which 18,723 were of males, and 23,421 of females. If, however, the deaths resulting from disease of the breast and generative organs are excluded, the male deaths are reduced to 17,820 and the female deaths to 14,112.

Referring to some of the other situations in which cancer is especially common, it will be found, according to the same Report,

that "the mortality of females from cancer of the upper portion of the alimentary canal, that above the stomach, is a small fraction only of that of males, but females suffer more from intestinal cancer. Disease of the stomach and rectum attacks males principally, but not at all with the overwhelming predominance applying from the œsophagus upwards. Cancer of the skin is also very much more fatal to males, but the excess is mainly due to disease of the penis and scrotum" These variations in the incidence of carcinoma in different situations in the two sexes are probably due, not to any inherent difference in the susceptibility of the tissues, but to their varying exposure to chronic irritation and other causes. Thus, the greater liability of the gall-bladder in the female must be considered in relation with the fact that gall-stones are much more common in that sex, and that in probably 80 or 90 per cent. of cases of cancer of this part, gall-stones are present.

Clinical course of a malignant tumour.—In view of the great diversity presented by the course of a malignant growth, dependent chiefly upon its nature and position, it is impossible to give any general description which is applicable to the different varieties. Beyond the fact that, unless successfully removed whilst in a localized condition, such widely different tumours as a soft round-celled sarcoma and a hard shrinking carcinoma will eventually destroy life, it is hardly possible to mention a single feature which is common to both. Certain popular fallacies with regard to a malignant tumour cannot be too often or too energetically exposed. These fallacies are: (1) That a malignant growth is necessarily painful; (2) that it makes rapid progress; and (3) that it is attended with loss of flesh and general deterioration of the health. All these evidences of malignancy may be conspicuous by their absence. Thus, to give a forcible example, the very common hard form of cancer of the female breast may present itself as an altogether insignificant small hard lump, unattended with pain or even discomfort, scarcely varying in size in many months or even several years, and unassociated with any recognizable effect on the nutrition or general health of the patient.

In the same way a small shrinking cancer of the pylorus may occasion a degree of ill-health not more marked than would be caused by an equal degree of pyloric obstruction due to a fibrous stricture. In the large majority of cases the recognition that a tumour is malignant must, in the early stages at least, when a correct diagnosis is of incalculable importance, be based upon the physical examination of the tumour itself and not upon the history of its growth or the general condition of the patient. Early loss of flesh is very rare unless from its position the tumour interferes with the normal processes of digestion For example, the emaciation caused by a carcinoma of the œsophagus

is in the early stages of the disease in direct proportion to the mechanical interference which it causes *with the act of deglutition*, and is no more marked than that which would be caused by an equal degree of interference dependent upon some non-malignant condition. It may, indeed, be laid down as a *rule that when an apparently early malignant tumour is associated with marked loss of flesh not caused by the mechanical effects of the tumour, the presence of metastases should be suspected, even though there be no physical signs to indicate their existence.* Absence of pain is, again, no proof that a tumour is benign in character. A want of knowledge of this fact too often explains the *patient's delay in seeking early medical advice*, and unfortunately sometimes leads the practitioner to fall into error. Thus, a carcinoma of the rectum may reach a most advanced stage without *causing even slight pain, or, in fact, any symptom to indicate that* serious disease exists, and the practitioner who is misled by this is likely to omit the only means of detecting the disease in its early stage, *viz. proper examination of the rectum. The special methods* available for the examination of such parts as the œsophagus, larynx, bladder, and lower bowel must never be neglected in a case in which *even the slightest suspicion exists that malignant disease of these* parts may be present. The rate of growth of a tumour is also of small value as a proof of malignancy. It is undoubtedly true that a soft cellular sarcoma usually increases rapidly, but many forms of carcinoma progress very slowly, and a rodent ulcer may, after even many years, attain only very small proportions. It may indeed be said that in the early stages there is no pathognomonic symptom of a malignant tumour.

Much importance was formerly attached *to the general deterioration* of health sometimes met with in malignant disease, and known as the *cancerous cachexia*. The condition is characterized by emaciation and anæmia, with often an *earthy, sallow tint of the skin, great weakness*, feeble pulse, loss of appetite, and temperature sometimes elevated, sometimes subnormal. From what has been already said, this condition *must not be regarded as* a special feature of the disease, but rather as an evidence of its advanced stage. Cachexia is particularly obvious when widely spread metastases are present, especially in the *viscera*; it is often the result of chronic septic poisoning such as occurs when ulceration of the growth has occurred, and is frequently intensified by the occurrence of *repeated hæmorrhages. Some of the* most distressing cases of this kind are those of inoperable carcinoma about the mouth and throat, associated perhaps with ulcerated masses of secondary *deposit in the lymphatic glands of the neck.*

The *duration of life* in untreated cases of malignant disease varies within the widest limits, for, whilst certain forms of sarcoma and

carcinoma may prove fatal in a few months, in some instances a carcinoma may be present for many years with very little interference with the general health. This is strikingly seen in many cases of rodent cancer of the skin; but even in the more common forms of the disease, such as cancer of the rectum and cancer of the breast, life may sometimes be prolonged for many years.

A study of the average duration of life, derived from statistical records of the different forms of malignant disease as it occurs in various situations, is of little practical value as a guide to foretelling the probable course of any individual case.

Death from malignant disease may mercifully result from progressive enfeeblement resulting from widely spread metastases, but too often it is preceded by a period of distressing pain and all the horrors of a fetid, discharging wound. Special complications too numerous to mention may hasten the fatal result, particularly when the primary tumour or its secondary deposits involve the respiratory or alimentary tracts.

In speaking of the natural course of a malignant growth, it has been stated that it tends continuously to extend, and finally to prove fatal. Such a result is, however, not absolutely constant, and there are on record a few authentic cases in which a malignant growth has undergone *spontaneous involution* and apparent cure. Before accepting a record of such a case as conclusive, it is essential that the tumour should have been examined histologically and its nature confirmed by a competent observer. Many cases are on record in which a tumour, apparently of a malignant nature, has disappeared. This has especially been noted in the case of certain abdominal tumours, which, after being examined by an exploratory operation and pronounced to be malignant and unsuited for removal, have subsequently subsided. It can hardly be doubted that in the majority of such cases the diagnosis was erroneous, for mimicry of malignant disease by various chronic inflammatory conditions is well known, the differentiation being impossible without the use of the microscope Godlee has recorded a case in which a hard tumour involving the gall-bladder was explored and pronounced to be undoubtedly malignant. Subsequently a gall-stone was passed from the bowel, and the tumour, which was certainly inflammatory, entirely subsided. We have ourselves put on record a case in which a large retroperitoneal tumour, having all the semblance of a hæmorrhagic sarcoma, gradually and completely disappeared after an exploratory operation. Evidence was, however, obtained which showed that the patient, a young man, was the subject of hæmophilia, and there can be little doubt that the "tumour" in this case was entirely the result of an extensive hæmorrhage behind the peritoneum. Every surgeon could cite similar instances from his

own experience, and their great importance in the consideration of reputed cures of malignant growths by various methods of non-operative treatment is obvious.

A remarkable instance of the spontaneous disappearance of an undoubtedly malignant growth has been recorded by Pearce Gould. The case was that of a woman whose left breast was removed in May, 1890, for a hard carcinoma, the nature of which was confirmed by microscopical examination. In July, 1892, the diseased axillary glands, and in February, 1894, recurrent nodules in the neighbourhood of the scar and one above the right breast, were removed. In December of the same year there were several fresh nodules, and the patient was dyspnœic. In January, 1895, at the age of 48, the patient was admitted to the Cancer Ward of the Middlesex Hospital; there were nodules on the chest wall, and enlarged glands in both axillæ and above the clavicles; there was dullness at the base of the right lung, and the general condition was very grave. In March, 1896, pain was complained of in the left thigh; the limb was shortened by one inch, and the femur below the trochanter was enlarged. In June, 1896, only *one small nodule was present in the skin above the scar resulting from* the removal of the left breast; there were no palpable glands; the dyspnœa had ceased, and the general condition had much improved; the left thigh was less painful. When shown at the Clinical Society of London in November, 1896, the patient was enjoying life; she walked with a limp, and, although the left lower limb was shortened by 1½ inches and the femur bent, the bone was not notably enlarged. As late as 1904 she was still continuing to enjoy good health. It is interesting to note that in this extraordinary case the catamenia ceased early in 1895, and that within a comparatively short time from this date the improvement in the patient's condition began.

Such a case as the above shows that a malignant growth shares with almost all other diseased processes a certain, although exceedingly slight, tendency to spontaneous involution.

Treatment of malignant tumours.—Except, perhaps, in the case of rodent ulcer, there is at present no means of treating a malignant tumour in the early stages of its growth which holds out a sufficient hope of effecting a cure to justify the surgeon in having recourse to it rather than in resorting at once to removal by operation, when the latter is practicable.

Operative treatment.—It will only be possible within the limits of this article to deal with certain general principles which should guide the surgeon in operating for the removal of a malignant tumour. The application of these to the treatment of malignant disease in its various forms and situations will be dealt with in the special sections

of this work, and will be here referred to only in order to illustrate the general principles.

1. Operation should be urged in any case in which a chronic lesion, especially of the skin or mucous membranes, presents any suspicion of incipient carcinoma. Histological examination will indicate whether or not it is necessary to advise a subsequent operation for the removal of the corresponding lymphatic area.

2. When it is necessary to establish the diagnosis by an exploratory incision into a tumour of doubtful nature, every care must be taken to prevent contamination of the wound by the tumour substance. The exploratory incision should be closed and the instruments used for the purpose discarded. When practicable, as, for instance, in the breast, the doubtful tumour should be cut out and then investigated, rather than explored by an incision into it *in situ*. If, as is, however, rarely the case, ordinary naked-eye examination fails to reveal the nature of the tumour, it may be possible rapidly to prepare a section and examine it microscopically with sufficient accuracy to enable the pathologist to advise the operator whether or not to proceed with the operation If the appearances are doubtful the question of further operation should be delayed until a more carefully conducted microscopical examination has been carried out.

3 The operation should be so planned as to remove not only the tumour itself, but such surrounding tissues as are known from experience to be especially liable to invasion by the growth, and it should be performed with as little roughness and dragging on the parts as possible, in order to avoid displacement of tumour cells into the veins and lymphatics.

4. The group of lymphatic glands receiving the lymphatics from the area in which the tumour is situated should in most cases be removed as freely as possible, whether they are palpably enlarged or not.

5 When possible, the excision of the primary tumour and the glands should be carried out at one operation, and the tissues between the two, in which infected lymphatic vessels are likely to be present, removed in their continuity. The chief exceptions to this rule concern those cases in which the primary tumour is so situated, as in the mouth, that rigid asepsis is impossible or cannot be ensured. In these circumstances the operation for the removal of the glands may with advantage be postponed with a view to preventing septic infection of the wound.

6. When a carcinoma arises in a part already the seat of certain precancerous changes, the operation must, if possible, be of such extent as to remove completely the altered part, as, for instance, in certain cases of carcinoma of the tongue and skin.

7. When the removal of skin is necessary, as in carcinoma arising in it or involving it by lymphatic extension, the amount removed must not be limited by the desire to close the wound as the final step in the operation. Immediate or subsequent skin-grafting may be employed when the closure of the wound is impossible.

The removal of a malignant tumour by any means other than the knife is very rarely practised. In a few instances the actual cautery, formerly much more extensively employed, is still used, as, for instance, by some operators in the removal of a carcinoma of the cervix of the uterus.

Mention must also be made of the use of high-frequency electric currents, or *diathermy*, in which a growth is removed by means of the heat produced in the tissues as the result of the resistance which they offer to the passage of the high-frequency current. This method is at the present time being somewhat extensively used, especially in the treatment of carcinomatous growths in the mouth.

In order that diathermy may be used safely and efficiently, numerous technical details, which need not be mentioned here, require attention. It will be sufficient to say that a large flat indifferent electrode is applied to the surface of the body, usually the back, and that the active electrode, by which the tumour is attacked, usually takes the form of a button or blunt knife. The button-shaped electrode is used for the direct destruction of a tumour, and the knife-like form for the removal of a growth by division of the tissue around it.

In malignant disease of the mouth it is urged in favour of diathermy that some growths, which from their extent and position are regarded as inoperable or only amenable to a very severe operation, can be removed by this method; pain after the treatment is usually slight, and as a rule healing proceeds rapidly. Hæmorrhage at the time of the operation can usually be avoided, unless an artery of considerable size is involved or the heating of the tissues is excessive, but there is some risk of secondary hæmorrhage at the period when the superficial sloughs are separating. It is some objection to the method that it is not possible to bring together the surfaces and edges of the wound by sutures, as can often be done after the excision of malignant growths of the mouth.

Operation for a malignant tumour may sometimes be justified, even when a cure is not obtained, if the patient's life is prolonged in a condition of comparative comfort, or, even when life is not prolonged, if the distress and suffering due to the primary growth is relieved.

[illegible] lines above indicated is giving an increased [illegible] ant disease, [illegible] guardedly.

No arbitrary time limit of freedom from recurrence—such as the three

years' limit suggested by Volkmann—can be adopted. It is undoubtedly true that in most cases in which recurrence takes place it ensues within the first year after operation, and that after the third year the prospect is very hopeful; but the period at which recurrence may ensue differs so widely in the different forms of malignant disease that, as Butlin points out, for some the three years' limit is too long, in some sufficiently accurate, and in others too short. Local recurrence means an incomplete operation, but visceral recurrences may take place when no evidence of their presence could be detected at the time of the operation. It has been suggested that late local recurrences may sometimes be explained by a new development of the disease rather than by incomplete removal of the original tumour. This may occasionally be true, but is usually disproved by the position of the recurrent growth. Thus, late recurrence may take place in the lymphatic glands without any recurrence *in situ*, as in the case of a woman whose breast was removed for carcinoma at the age of 56. Two years later a recurrent growth was removed from the axilla, and death occurred at the age of 70, with recurrence in the glands of the neck.

Treatment of inoperable malignant tumours.—It is scarcely necessary to remind the reader that the treatment of malignant tumours by non-operative measures has always enjoyed a very undesirable degree of notoriety in the hands of quacks and other irregular practitioners, and that every question bearing upon this important subject must be approached with an open mind. In view of the extreme difficulty of the early recognition of the disease, it is not surprising that cases can easily be collected which appear to illustrate the successful use of almost every conceivable variety of the so-called "cancer cures." Such cases will not bear scientific investigation, and to prove that a malignant growth has been effectually cured by any form of treatment it is first necessary to prove that a malignant growth actually existed. It must further be remembered that in advanced inoperable cases, in which alone non-operative methods are justifiable, considerable improvement in the patient's general condition, and even in the condition of the tumour itself, may result from careful nursing and dieting and the suitable treatment of ulcerated growths.

It is impossible even to enumerate the many methods of treatment which have from time to time been honestly thought to be of benefit in the treatment of malignant disease, and it must suffice to refer shortly to those methods which may at the present day be tried in cases in which, for various reasons, operation is impracticable or in which recurrence after operation cannot be further dealt with.

In this connexion the first place must be given to **irradiation**

by X-rays and radium, but, although the action of these agents upon certain forms of new growth is very remarkable, the whole subject must still be considered to be in the experimental stage. At present the evidence *does not justify the use* of irradiation in the treatment of an operable malignant tumour, except in the single instance of rodent ulcer, and thus, in view of the nature of the cases in which X-rays and radium are employed, the results cannot fairly be contrasted with those obtained by operation in favourable cases. The circumstances in *which irradiation is employed in the treatment* of malignant tumours are the following: (1) For inoperable tumours; (2) for metastases and for local recurrences after operation; (3) as a preliminary treatment before operation with the object of destroying tumour cells which may be present in the tissues to be divided at the operation; and (4) *subsequently to operation with the object* of preventing local recurrence.

The choice between X-rays and radium is in practice partly determined by the fact that whereas full doses of X-rays are usually available, radium is often not obtainable, or only in very small amount; but, apart from this, it is believed by some authorities that the rays of radium are more effective than X-rays in similar amount. Speaking generally, it may *be said that* X-rays are chiefly employed when it is desired to irradiate a large area, especially for a superficial growth, while radium is preferable for the treatment of a deeply seated growth or for a superficial one of very limited area.

Of the different rays given out by radium—the α, β, and γ rays—*the γ rays are those chiefly employed for therapeutic purposes,* and in order to filter off the less penetrating α and β rays and prevent damage to the superficial tissues, it is the custom, *following the method* of Wickham and Dominici, to interpose varying thicknesses of lead or platinum between the radium and the part to which it is applied.

Experiments have shown that the effects of irradiation on the *cells of a tumour vary according to the dose.* Thus, whereas a full dose causes necrosis of the tumour cells and renders the tumour no longer inoculable in a living animal, *smaller doses* may merely retard the growth, while there is some evidence that still smaller doses may have a stimulating effect. It is thus essential that in the treatment of a malignant growth a full or lethal dose should be applied. Further, it is possible that while the intensive effect on a limited area *is destructive*, the feeble effect on more distant parts may be stimulating. It is for this reason that in certain circumstances X-rays may *be preferable to radium on account of* the large area readily brought under their influence, and that the combined use of X-rays and radium may sometimes be advantageous.

The histological changes which have been observed in malignant tumours exposed to a lethal dose of radium or X-rays consist in necrosis of the cell elements and proliferation of the connective tissue, which results eventually in the formation of a cicatrix.

A very marked difference is noted in the behaviour of different malignant tumours to treatment by irradiation. Those in which the results have been most striking are basal-cell carcinoma of the skin (rodent ulcer), some forms of sarcoma, especially endothelial sarcoma and lympho-sarcoma, and carcinoma of the cervix of the uterus. Less striking results have been obtained in carcinoma of the breast and rectum and sarcoma of bone; whilst in melanotic sarcoma and in squamous carcinoma in all situations the results have, on the whole, been very disappointing. It is worthy of notice that in some cases the use of X-rays, whilst having no striking effect on a tumour, may nevertheless be followed by considerable relief of pain. Among the many questions requiring further investigation is the possible increased liability to metastases following irradiation of a malignant growth. Kellock and others have recorded interesting cases bearing on this question, and it is worthy of mention that in the case of carcinoma of the uterus of which the pulmonary metastases are illustrated in Fig 108 (p. 491), treatment with radium had been adopted.

In carrying out treatment by irradiation, many technical details concerning dosage, screening, frequency of application, etc, require attention, but can only be very shortly mentioned here.

In using X-rays a full dose at intervals has, on the whole, appeared to yield the most encouraging results. Radium can be employed in the form of the hydrated bromide contained in a lead or platinum tube or spread out by means of a special varnish on an applicator, or in the form of the emanation contained in a glass tube. When practicable, the tube of radium should be embedded in the substance of the tumour through an incision

Seitz and Wintz of Erlangen have recently elaborated an intensive X-ray treatment in which great penetrating power is obtained for the treatment of deeply seated growths. By the use of two similar coils in series a very penetrating ray is obtained which is only to a small extent cut off by the tissues superficial to the growth. The results of the use of this method have so far been encouraging.

Coley's fluid.—The effects of the use of the mixed toxins of the *Streptococcus erysipelatis* and *Bacillus prodigiosus* in cases of inoperable sarcoma certainly seem to justify a continued trial. The treatment is founded on the fact that malignant tumours, especially sarcoma, have been known to disappear after attacks of accidental erysipelas. This induced Fehleisen in Germany and Coley in New

York to inoculate with erysipelas patients suffering from malignant growths; and later, in 1892, Coley first experimented with a culture of the erysipelas streptococcus sterilized by heat and filtration. He found that a febrile reaction followed the injection, and that a temporary inhibitory action was observed on the growth of malignant tumours. Roger subsequently showed that if the *Bacillus prodigiosus* was grown together with the erysipelas streptococcus the virulence of the latter was increased, and as the result of this observation Coley experimented with the mixed toxins—*Coley's fluid* consisting of the two cultures in definite proportion, sterilized by heat, and with the addition of glycerine and a small quantity of thymol. After injection of the fluid, either into the tumour or elsewhere, Coley has observed that the tumour becomes at first paler and more movable, whilst, later, areas of softening due to caseous degeneration occur in it, and finally in a successful case the tumour gradually disappears by absorption or by breaking down and liquefaction. He has used the treatment in all forms of sarcoma, except melanotic growths, and has employed it in certain cases of operable sarcoma of the long bones in which only an extensive amputation would be available, and also after operations for sarcoma with a view to the prevention of recurrence. In carcinoma the results have been disappointing. Coley advises that the treatment should be commenced with an injection of a fourth of a minim into the buttock or over the pectoral muscle, and that the injection should be repeated daily with increasing doses until a febrile reaction of 102°–104° F. is obtained, the maximum dose being 8½ minims. If the patient is not very susceptible, small injections may also be given into the tumour, should its position allow. After the tumour has entirely disappeared the injection should be continued in smaller doses and at longer intervals for three or four months. According to Coley, the risk is small, the chief danger being the injection of too large an initial dose into a vascular tumour. Between 1890 and 1919 Coley had treated 250 cases of sarcoma of the long bones by this method, the use of the mixed toxins being in many instances combined with the local application of radium. He advises that, if the tumour does not show distinct improvement in the course of four or five weeks amputation should, when practicable, be performed and the treatment continued as a prophylactic against recurrence. The evidence of the value of the treatment in Coley's hands seems to be conclusive, and the disappointing results which have hitherto been obtained in this country may perhaps in part be explained by improper preparation of the fluid, and an unwillingness on the part of surgeons to continue a treatment which is attended with much discomfort to the patient.

SARCOMA

A sarcoma is a malignant non-epithelial tumour. Although differing widely in the details of their minute structure, the sarcomas all consist of cells of the connective-tissue type, and these cells may be of a single uniform shape, or the same tumour may consist of cells of different kinds. The sarcoma cells present forms which find their prototypes in the various changes which undifferentiated round cells undergo in their development into fully formed connective tissue. Thus the cells may be round, oval, or spindle in shape, and, as in all rapidly growing cellular formations, multinucleated cells are not uncommon. The cells of a sarcoma do not lie in actual apposition, but are separated by a varying amount of ground substance, which may be homogeneous, granular, or fibrillated.

The blood-vessels in a sarcoma are usually abundant, and are embryonic in character, partaking rather of the nature of blood clefts and spaces than actual vessels. They present the characters of blood-vessels in the process of development, consisting of channels surrounded by cells which may resemble delicate endothelium, or may be indistinguishable from the essential tumour cells themselves. For instance, in the spindle-cell variety the vascular spaces may be bounded merely by spindle cells arranged end to end in immediate relation with the surrounding spindles of the tumour. A further point of importance in the vascular arrangement in a sarcoma is the fact, which naturally follows from what has been said, that the blood channels run actually among the cells of the tumour (Fig. 103, p 485). This arrangement is important as explaining the readiness with which the tumour cells enter the blood-stream and occasion metastases, and also affords valuable help in endeavouring to distinguish malignant tumours of the connective-tissue type from others of an epithelial type For instance, certain round-cell sarcomas may present close histological resemblances to some forms of spheroidal-cell carcinoma. Among other means of differentiation, it will be noted that in the sarcoma blood channels are seen passing actually among the tumour cells, whereas in the carcinoma the blood-vessels are limited to the connective-tissue stroma and in no case pass into the masses of spheroidal cells.

It will thus be seen that a sarcoma may be regarded as a tumour composed of connective tissue of an embryonic type, in the character not only of the cells but also of the blood-vessels.

The practical difficulty which often presents itself to the pathologist is to distinguish by histological examination between sarcoma and many cellular formations of an inflammatory or reparative nature, in which connective-tissue development is in progress. For instance,

a microscopic section of a small round-cell sarcoma closely resembles that of simple granulation tissue. Both consist of undifferentiated round cells and undeveloped blood-vessels. *From the examination* of a fragment of such tissue, the distinction may be practically impossible, but a wider examination will usually reveal the essential difference—that, whereas in granulation *tissue its progressive conversion* into fibroblasts and fully formed connective tissue can be demonstrated, in the sarcoma all parts present the undeveloped stage, and show no *tendency to pass on to a higher grade of* development.

The great variations in structure presented by the malignant connective-tissue tumours are dependent partly upon the character of the sarcoma cells and partly upon the presence of different forms of connective tissue, which may be associated with the sarcoma cells as an essential constituent of the tumour. The following classification is based upon these characters:—

Sarcomas differing in the character or arrangement of the cells—
1. Round-cell sarcoma.
2. Oval- or spindle-cell sarcoma.
3. Mixed-cell sarcoma.
4. Endothelial sarcoma (malignant endothelioma).
5. Melanotic sarcoma.

Sarcomas characterized by the special nature or arrangement of the stroma—
1. Lympho-sarcoma.
2. Fibro-sarcoma.
3. Myxo-sarcoma.
4. Chondro-sarcoma.
5. Osteo-sarcoma.

We shall consider first *the sarcomas which differ in the character or arrangement of the cells.*

1. **Round-cell sarcoma.**—In describing this tumour, little need be added to what has already been said (p. 485). *In its typical form* the tumour consists entirely of small round cells resembling lymphocytes, separated by a small amount of homogeneous or finely granular ground-substance. The vascularity of the tumour is often great, and the blood is contained in vessels resembling embryonic capillaries among the tumour cells (Fig. 109).

2. **Oval- and spindle-cell sarcoma.**—*In this variety of* sarcoma the cells vary in form between short ovals and long slender spindles, and the nuclei correspond in shape. In the spindle-cell sarcoma the spindles are not always *irregularly arranged*, but in parts of the tumour will often be seen to be collected into fasciculi which

intersect in various directions. It thus happens that in a section of the tumour different fasciculi will be divided in different directions, longitudinally, obliquely or transversely, and as a result the appearance may at first sight suggest that the spindle cells are mixed with oval and round cells (Fig. 110). The blood spaces in a spindle-cell sarcoma consist of channels bounded by spindles arranged end to end and often indistinguishable from the other cells of the tumour.

3. **Mixed-cell sarcoma.**—The variations in the size and shape of the cells in many sarcomas are so great that such tumours can

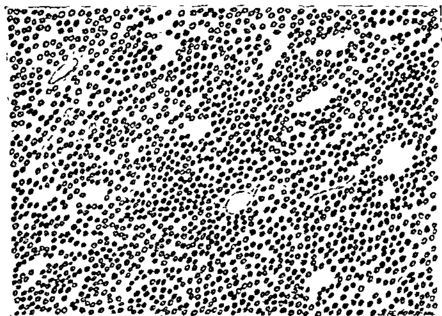


Fig. 109.—Microscopic section of round-cell sarcoma.

only be grouped together in one class. In many, however, the preponderance of one kind of cell is so marked that the characters of the growth are determined by it, and it may be considered rather as a slight variation of the round- or spindle-cell variety. In any rapidly growing form of sarcoma it is not uncommon to find a number of multinucleated cells present, and sometimes these may be so numerous as to justify the name *giant-cell sarcoma.* Such a tumour must be carefully distinguished from a myeloma, which, although formerly included among the sarcomas, is now by most pathologists regarded as a form of benign growth (p. 432).

The naked-eye characters of the round-cell, the spindle-cell, and the mixed-cell forms of sarcoma may most conveniently be considered together, for often the differences are not sufficient

to enable a conclusion *to be drawn as* to the *histological* structure. A typical round-cell sarcoma is usually very soft, and the tumour substance is homogeneous and white, yellowish-white, or pinkish-white in colour. The appearance is often strikingly like that of white brain-substance, and, although a similar appearance may be presented by some very soft forms of spheroïdal-cell carcinoma, it is certain that in the majority of cases the "encephaloid cancer" of the older writers was a round-cell sarcoma. *A typical spindle-cell* sarcoma, for instance, of the periosteum of a long bone often

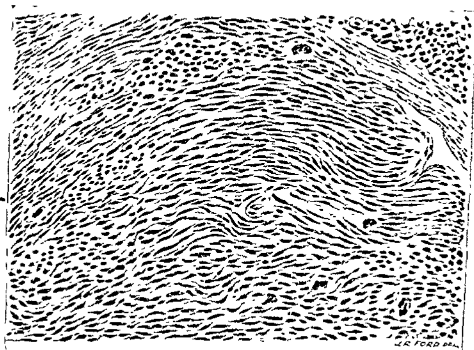


Fig. 110.—Microscopic section of spindle-cell sarcoma.

presents a distinctly striated or fibrillated appearance in section, which contrasts with the noticeably *homogeneous consistence of* the round-cell form (Fig. 125). This appearance is explained by the arrangement of the spindle cells in *intersecting fasciculi. Some* spindle-cell sarcomas, such as those of the skin, are firm in consistence and, to the naked eye, look more like fibromas

Sarcomas of the varieties under consideration are very liable to degenerative changes, especially as *the result of hæmorrhagic extravasation* into their substance. In some instances this may be so marked that the whole tumour resembles little more than a mass of blood-clot or a blood cyst. Fatty degeneration may result in the

presence of yellow areas in the tumour, and may also lead to the formation of cysts. When a sarcoma is examined together with the surrounding tissues the infiltrating character of the tumour is usually sufficiently obvious, for, although its outline is often sharply defined, the neighbouring tissues are inseparably connected with it. This is often strikingly seen in the relation of the muscles to the surface of a periosteal sarcoma. It is, however, not unusual to find that around the tumour there is a distinct attempt at encapsulation, but, unlike the capsule of a simple tumour, the fibrous layer surrounding a sarcoma is intimately adherent both to the surrounding tissues and to the tumour substance

4 **Endothelial sarcoma (malignant endothelioma).** —In considering the structure and characters of the endotheliomas, it was pointed out that it is difficult to draw a sharp line between simple tumours of this nature and certain tumours of a malignant type. To the latter the name "malignant endothelioma" has sometimes been applied, but the designation "endothelial sarcoma" seems more accurate. In some cases the structure of a tumour which is obviously malignant cannot be distinguished from that of a simple endothelioma (p 452). In other tumours it will be found that in some parts the growth has the characteristic structure of an endothelioma and in other parts the structure of a purely cellular sarcoma Such a mixed structure strongly suggests that a malignant transformation of a simple endothelioma has occurred, and this view is supported by clinical evidence. Thus, it not uncommonly happens that a tumour, after a prolonged and apparently benign course, may take on a more rapid rate of growth and assume the local and general evidences of malignancy.

In the group of endothelial sarcomas may also be placed certain special forms of sarcoma, the cells of which are arranged in such a way as to suggest an endothelial or perithelial origin. Of these, the most important is the **angio-sarcoma** or **plexiform sarcoma**, such as occurs in the pia, arachnoid, eye, and elsewhere. Microscopically such a tumour consists of capillary vessels bounded by large spheroidal cells in several layers. By a further proliferation of the spheroidal cells the meshwork of the vascular network becomes completely occupied by solid cell masses separated by the capillaries, with possibly a slender reticulum of connective tissue. To this variety the name **alveolar** or **large round-cell sarcoma** is applied. It is not uncommon in the skin and subcutaneous tissue, and in its histological features closely resembles an undifferentiated carcinoma (Fig. 111).

In some tumours of this group the cells are arranged in radiating fashion around a central vessel, and evidently arise from the endothelium of the adventitia or of the perivascular space. From these

cells a network of slender columns extends into the surrounding tissue. This variety is known as a **perithelial sarcoma.**

In the angio-sarcoma the walls of the vessels sometimes undergo hyaline degeneration, producing the tumour known as a **cylindroma.**

5. **Melanotic sarcoma.**—This variety of sarcoma is characterized by the presence of a pigment, known as melanin, in the cells. Melanin is an iron-free pigment containing sulphur; it occurs in



Fig. 111.—*Microscopic section of alveolar sarcoma of neck.*

the form of highly refracting amorphous granules in the protoplasm of the cells, and may collect in such amount as to enlarge the cell and completely obscure its structure. Under the microscope the granules usually present a bright yellowish-brown colour, but to the naked eye the growth may, in parts at least, be quite black. Melanin is supposed to be a derivative of the proteid molecule, and must be distinguished from changes resulting in hæmoglobin. In patients suffering from melanotic tumours it has sometimes been noticed that the urine becomes dark after exposure to the air, as the result of the oxidation of a substance known as melanogen.

In many melanotic sarcomas the cells vary in shape, oval cells or

short spindles usually predominating (Fig. 112). In another form, especially that beginning in the skin, the cells are large and rounded or polyhedral, and tend to assume a more or less distinctly alveolar arrangement. This arrangement suggests that the cells are either endothelial or epithelial in origin, or, in other words, that the tumour is either an endothelial (or alveolar) sarcoma or a carcinoma. Upon



Fig. 112.—Microscopic section of melanotic sarcoma.

this and other considerations has arisen much discussion as to the true nature of melanotic malignant growths, and, whilst they were formerly classed among the sarcomas, the view is now rather widely held, following Unna and others, that they are really melanotic carcinomas. In the skin, tumours of this class not uncommonly arise in pigmented moles, and thus the question of their nature is closely connected with the question of the nature of the "nævus cells" of moles, in which they apparently arise (p. 480). Whilst fully recognizing the difficulty of the subject, we are of opinion that the evidence is in

favour of the view that the malignant melanotic tumour, of the skin at least, is a sarcoma.

Melanotic sarcoma occurs chiefly in the skin and the eye, and the characters of the disease will be *considered as it occurs in these situations* (pp. 524 and 542); it has also been described in the central nervous system, the nasal cavity, the palate, the lower part of the rectum and the anus, and in the vulva and vaginal orifice. In the case of melanotic sarcoma of the palate illustrated in Fig. 113 the growth rapidly recurred after operation and invaded the maxillary antrum. Melanotic malignant tumours are also not uncommon in horses, especially greys.

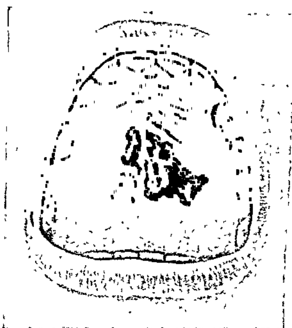


Fig. 113.—Melanotic sarcoma of palate.

A short description will now be given of *those varieties of sarcoma which are characterized by special features of the stroma* with which the sarcoma cells are associated.

1. **Lympho-sarcoma.**—This is a small round-cell tumour in which the cells are contained in a delicate reticulum formed by the branching processes of other cells. The structure thus closely resembles that of normal lymphoid tissue, and it is in such tissue only that the lympho-sarcoma arises. It may thus occur primarily in lymphatic glands, mucous membranes, and other structures, such as the tonsil, in which lymphoid tissue is normally present. When occurring primarily in lymphatic glands, as for instance in the mediastinum, a rapidly growing tumour of large size may result. In Fig. 114 is illustrated a case in which a primary lympho-sarcoma of the tonsil was associated with extensive deposits of growth in the cervical lymphatic glands. In rare instances secondary deposits may occur in the bones, skin, and elsewhere.

2. **Fibro-sarcoma.**—Examined microscopically, a fibro-sarcoma is most commonly of the spindle-cell variety, the fasciculi of spindles being separated by a more or less considerable amount of ordinary

fibrous tissue. Less commonly, the cell elements are of rounded or mixed shapes, and the masses of cells are irregularly distributed in the fibrous *stroma*. The *fibrous tissue may* be relatively so abundant that the naked-eye characters of the tumour are indistinguishable *from those of a fibroma, and even by histological examination it may* be impossible to draw a clear distinction between a fibro-sarcoma and a soft, unusually cellular fibroma. This is of much clinical importance, and it not infrequently happens that a tumour regarded in the first instance as a fibroma shows by its recurrence, especially locally, that it is decidedly malignant.



Fig. 114.—Lympho-sarcoma of glands of neck, secondary to primary tumour in tonsil.

3. **Myxo - sarcoma.**—In this variety a considerable ad*mixture of myxomatous tissue* is present. The sarcoma cells are usually of the *small, round* variety, and are arranged in masses separated by areas in which the branching cells of the myxomatous tissue are recognizable. The tumour is very soft, and presents to the naked eye and microscope an appearance closely resembling that of a pure myxoma, or pale semi-translucent areas may be visible in the more opaque sarcomatous tissue. Myxomatous tissue is *often present in a chondro-*sarcoma.

In *some cases of myxo-*sarcoma the tumour may reach a very large size, pursuing at first a slow course, but recurring locally after removal without the production of metastases In a recent case of this kind in University College Hospital the tumour, which was a second recurrence, formed an enormous mass extending among the extensor and adductor muscles of the thigh. The primary tumour and the first recurrence had been removed several years previously. Two specimens of similar myxo-sarcomatous tumours of the thigh are preserved in the Museum of the Royal College of Surgeons.

4. **Chondro-sarcoma.**—In this variety the cartilage may be present only in the form of small islands in a tumour which is otherwise purely cellular, or it may so preponderate that the *tumour* has

the macroscopic characters of a simple enchondroma. In the latter case a careful microscopic examination will serve to indicate the true nature of the growth, for, whereas in a simple cartilaginous tumour the lobules of cartilage are held together by strands of connective tissue, in the chondro-sarcoma the tissue intervening between the cartilage lobules presents the cellular characters and vascular arrangement characteristic of a sarcoma, and the two tissues may pass gradually one into the other (Fig. 115).

5. **Osteo-sarcoma.**—The variations in the amount of ossification present in this form of sarcoma are comparable with the varying degrees of chondrification in a chondro-sarcoma. Thus, in some

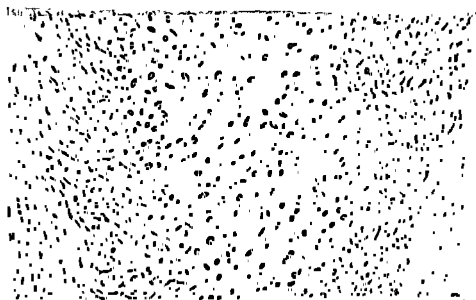


Fig. 115.—Microscopic section of chondro-sarcoma of femur.

tumours the presence of bone is only discovered on microscopic examination, or perhaps by the detection of fine gritty spots with the point of a scalpel, whereas in other tumours it is so extensive that the tumour partakes of the naked-eye characters of a simple osteoma. The bony trabeculæ often present evidences of irregular deposition and absorption, the former by the presence of osteoblasts on the surface, and the latter by the presence of multinucleated osteoclasts lying in Howship's lacunæ. The spaces in the osseous tissue are occupied by characteristic sarcoma cells, which are usually spindle-shaped or of mixed form (Fig. 116).

The **clinical features** of a sarcoma differ so widely according to its position and variety that no single description of the tumour

is possible. A sarcoma of a deep structure, such as the periosteum, or a muscle or fascia, presents itself as a tumour which continuously increases in size, often at a rapid rate. It tends to assume a more or less globular shape, and is often distinctly lobulated. Its consistence varies greatly, and, while the softer forms may easily be mistaken for a fluid swelling, the firmer varieties may closely resemble

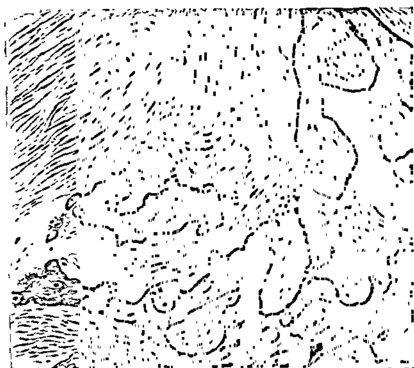


Fig. 116.—Microscopic section of osteo-sarcoma of femur.

a fibrous tumour in their consistence. The frequent resemblance of a soft sarcoma to a fluid swelling is most important in diagnosis, especially in the differentiation of such a tumour from a chronic abscess, *for the softness may be so marked that a distinct sense of* fluctuation can be detected in it. The differentiation is sometimes rendered more difficult by the fact that some local heat is often appreciable over the tumour, and in certain cases by a distinct elevation of the body temperature.

A physical sign of great diagnostic importance which not infrequently can be detected in a vascular sarcoma is *pulsation*. This sign is often very helpful, especially as a means of distinguishing a sarcoma of a bone from an inflammatory enlargement, but it is also

an occasional cause of error, and a pulsating sarcoma of the ilium has been known closely to simulate an iliac aneurysm, or a similar tumour of the upper end of the humerus an aneurysm of the axillary artery.

Careful examination will usually show that the pulsation of a sarcoma does not possess the strikingly expansile character of the pulsation of an aneurysm, nor does the tumour behave in the same way as an aneurysm when the main vessel above it is compressed. The pulsation is not so completely controlled, and the tumour does not diminish in size like an aneurysm, filling out again with bounding pulsations when the pressure on the vessel is removed. Occasionally a bruit may be audible in a vascular sarcoma.

When a sarcoma becomes superficial the cutaneous veins are often enlarged and congested. As the surface of the tumour reaches the skin the latter becomes gradually thinned over it, and eventually, after assuming a bluish-red colour, ulcerates, and the tumour itself is exposed and at once proceeds to fungate through the opening as a soft vascular mass which discharges a thin blood-stained fluid. The mode of invasion of the skin by an underlying sarcoma may be contrasted with that of a deeply seated carcinoma—for instance, of the breast. In the sarcoma the skin becomes thinned, shiny and discoloured, and finally ulcerated, in the carcinoma the skin becomes thickened, adherent to the tumour, and often covered with thick epidermic crusts before at last actual ulceration occurs. After ulceration the sarcoma protrudes as a fungating hæmorrhagic mass, while the carcinoma, as the result of necrosis of the tumour substance, forms an irregular excavation surrounded by a characteristic hard, raised, and often everted border.

The **metastases** of sarcoma occur, as already stated, chiefly by the blood-stream, and are thus most common in the lungs. The secondary growths show a striking tendency to reproduce in all its details the structure of the primary tumour, and the appearance of masses of chondrifying or ossifying sarcoma in the lungs forms a very remarkable picture. *Although the tendency to invasion of the lymphatic glands* is much less common than in carcinoma, the difference in the behaviour of the two classes of malignant growth in this respect is only a relative one, and in many cases of sarcoma, especially in certain situations, *secondary deposits* in the lymphatic glands will be found.

Although the metastases by way of the blood-stream are most common in the lungs, they may also occur in the abdominal viscera, the bones and skin, and in rare cases a generalized sarcomatosis occurs. Metastases sometimes result from the direct extension of the primary tumour into a neighbouring vein. Thus, a sarcoma of the kidney may extend through the renal vein into the vena cava, and in some forms

of abdominal sarcoma the implication of the portal vein or one of its tributaries in this way is followed by secondary deposits in the liver.

The **diagnosis** of sarcoma must for the most part be left for consideration when the disease is described in special situations, and only a few points having a general bearing on the subject can be mentioned here. The difficulty which presents itself is more often concerned with the differentiation of sarcoma from various inflammatory conditions than from other forms of new growth. Thus, a soft, deeply seated sarcoma may, in its clinical features, closely resemble a chronic abscess. Again, a syphilitic gumma—for instance, of a muscle—may so closely resemble a sarcoma that only the fact that the tumour steadily increases in spite of antisyphilitic treatment serves to suggest the more serious nature of the case. Sarcoma of a bone in its early stages may be clinically indistinguishable from several conditions of an inflammatory nature, such as a central abscess and various forms of osteitis and periostitis, resulting especially from syphilis and tuberculosis.



Fig. 117.—Melanotic sarcoma of palm.
(*From the New Sydenham Society's Atlas of Pathology*)

In doubtful cases the detection of pulsation may be of the greatest importance in diagnosis, and may indeed prove to be the only ground upon which a correct conclusion is to be based.

As a last means of diagnosis an exploratory incision into the doubtful swelling must be made.

Situation.—Being a malignant connective-tissue growth, a sarcoma may arise wherever connective tissue is present, and is thus almost unrestricted in its possible sites of origin. Certain situations are, however, especially liable, and it will be convenient to consider separately sarcomas as they occur in the skin, subcutaneous tissues and fasciæ, muscles, nerves, bones, mucous membranes and sub-

mucous tissue, serous membranes *and subserous tissue, and solid* organs (the kidney, ovary, uterus, breast, etc.).

Sarcoma of the skin usually occurs as the spindle-cell or the fibro-sarcomatous form, or as the variety of *endothelial sarcoma* known as alveolar sarcoma. *Spindle-cell sarcoma* or *fibro-sarcoma* usually begins as a small, flattened, firm tumour to which the smooth epithelial layers are intimately adherent. As the tumour increases, secondary nodules, sometimes in considerable numbers, may develop around it, but the primary tumour *itself* rarely reaches a large size. Ulceration, if it occurs, only involves the surface of the growth. In this *form of sarcoma the lymphatic glands are not* usually invaded, and the malignancy of the tumour chiefly shows itself locally; recurrent nodules in the skin *surrounding the cicatrix* are likely to appear even after an apparently very free removal.

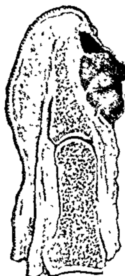


Fig. 118.—Subungual melanotic sarcoma.

(University College Hospital Museum)

Numerous cases of *alveolar sarcoma* of the skin are on record. The tumour begins as a firm *nodule in the cutis, which steadily enlarges* and soon ulcerates. In common with other forms of cutaneous sarcoma, this variety also tends to be followed by secondary nodules in the surrounding skin, and Erichsen mentions a case in which twenty or more such tumours, varying in size from a pea to a walnut, were present on the skin of the leg. Sooner or later visceral metastases *are likely to occur.*

Melanotic sarcoma of the skin is most common on the hands and feet, but, especially as the form which arises in a pigmented mole, it may occur in any part of the cutaneous surface. Sometimes the growth originates in a scar *such as that left by a punctured wound*, as in a case recorded by Eve, in which the tumour formed in a scar in the sole of the foot resulting from a wound twenty years previously. It generally begins as a small pimple or patch of a brown or black colour and, as it slowly increases, forms a raised and sometimes lobulated or slightly pedunculated tumour. *Eventually ulceration occurs* and the tumour forms a fungating mass in which the pigmentation may be very evident (Fig. 117), but is sometimes so slight that the tumour *may readily* be mistaken for an ulcerated squamous carcinoma. Around the primary tumour secondary nodules, sometimes in large numbers, may appear in the skin, or *the secondary deposits may take* the form of small brown or black stains.

Another important variety is that which arises at the edge of the matrix of the nail as a narrow brownish stain. After ulceration has occurred the nail may separate, and the condition may thus closely resemble some forms of paronychia. For this reason Hutchinson suggested the name *melanotic whitlow* (Fig. 118).

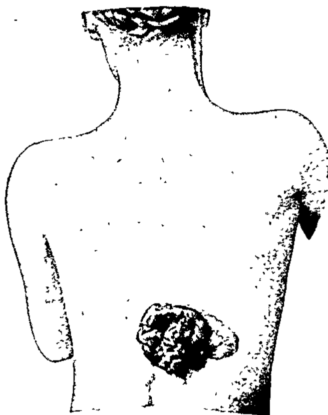


Fig. 119.—Melanotic sarcoma arising in a pigmented mole of the skin of the back.

(*From a case under the care of Christopher Heath*.)

The malignant transformation of a pigmented mole may be evidenced by the occurrence of ulceration, by an extension of the pigmented area, by the growth of a raised tumour from its surface (Fig. 119), or, without any striking change in the mole itself, by the enlargement of the neighbouring lymphatic glands.

The section of a melanotic sarcoma varies much in its naked-eye characters. Sometimes it is uniformly black in colour, but more frequently the pigment is present in the form of brown or black patches or streaks in the pinkish-white tumour substance, or may be limited

to certain lobules of the growth (Fig. 120). The extreme malignancy of melanotic sarcoma is universally recognized, and, while the primary growth in the skin still remains an inconspicuous and sometimes undetected pigmented spot, extensive deposits of growth may already have occurred in the lymphatic glands, and metastases may be widely distributed in the viscera and bones. To a certain extent, no doubt, the excessive tendency to metastasis is apparent rather than real because of the fact that even minute deposits are so easily recognized with the naked eye, but, even allowing for this possible fallacy, there is no doubt that melanotic sarcoma is a most malignant tumour. The investigations of Handley show that even in its earliest stages the tendency to widespread lymphatic invasion is so great that very free removal of the tissues around the primary growth and the infected glands is necessary.

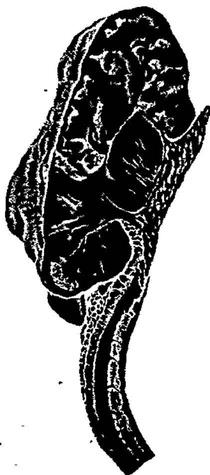


Fig. 120.—Section of the melanotic sarcoma illustrated in Fig. 119.

Sarcomas of the subcutaneous tissues or **deep fasciæ** may occur in almost any part of the body, and vary widely in their histological structure and clinical features. The small round-cell variety is the most malignant, and may rapidly assume a large size, presenting in its earlier stages the characters already described (p. 521), and eventually, after ulceration of the overlying skin, producing a large fungating mass, from which repeated hæmorrhages may occur (Fig. 121).

Sarcoma of muscles is very rare, but is the most common tumour occurring primarily in this situation. It is probably more frequent in the muscles of the lower extremity than in those of the upper, and has been met with more often in the proximal than in the distal parts of the limbs. According to Butlin, the

pectoralis major, biceps, and sartorius are the muscles most often affected. The round-cell sarcoma is probably most frequent. The tumour may reach a large size while still entirely surrounded by the fascial sheath of the muscle, but when the growth extends beyond this it rapidly involves the surrounding part. Glandular enlargement is exceptional, but metastases in the viscera have been recorded. In its early stages a sarcoma of muscle is likely to be confounded with a syphilitic gumma, which is not uncommon in muscular tissue.

The course likely to be pursued by a sarcoma of muscle is well illustrated by the following case: A girl aged 15 noticed a small lump in the calf of the right leg Two months later the tumour, as large as a plover's egg, was removed together with the surrounding part of the gastrocnemius muscle in which it was situated, and proved to be a small round-cell sarcoma. Two months later extensive recurrence had taken place in the calf muscles, and amputation was then performed through the thigh. When seen again, five months after amputation, the patient was suffering from fever and dyspnœa; two pints of blood-stained fluid were removed by aspiration from the left pleural cavity. It was thus clear that metastases were present in the lungs, and that a fatal result would not be long delayed.



Fig. 121.—Sarcoma of neck.
(From a case at University College Hospital)

The **treatment** of a sarcoma of muscle by the complete removal of the muscle, as originally suggested by Teevan, is rarely practicable even if advisable, and in the case of the limb-muscles high amputation is the only alternative. When the muscles in the region of the shoulder are involved, the interscapulo-thoracic amputation must be performed.

Sarcoma occasionally occurs in the muscular substance of the **tongue**, and cases of this nature have been recorded by Butlin,

Targett, Marion, Littlewood, and others. The disease usually begins in the substance of the tongue, while the mucous membrane over it remains intact. Most of the recorded cases have been of the round-cell variety, and enlargement of the lymphatic glands appears to be exceptional. Lympho-sarcoma of the base of the tongue has, however, caused extensive glandular involvement. A sarcoma of the substance of the tongue must be carefully distinguished from such inflammatory affections as gumma, chronic abscess, and actinomycosis, and from a simple angioma.

Endothelioma of the tongue has been described by Lazarus Barlow and Eve. In Eve's two cases, which should be regarded as instances of endothelial sarcoma of low malignancy, the tumour formed a prominent elevation at the extreme base of the tongue, and there was some glandular enlargement. In one case the tumour was of a lymph-endotheliomatous, and in the other of a perithehomatous, type.

In a case of this nature which we have observed in a woman aged 42, the tumour, which had only been noticed for a month, formed a smooth prominence at the back of the tongue, chiefly to the left side of the middle line. A considerable glandular enlargement in the right carotid triangle had existed for at least two years. The tumour of the tongue and the glandular deposit both presented a structure which was at first thought to be carcinoma, probably arising in the mucous glands, but further examination and a comparison with the report of Eve's case have convinced us that the tumour was an endothelial sarcoma with mucoid degeneration in the centre of the cell masses.

In speaking of non-ulcerated tumours at the back of the tongue it may not be out of place to refer to the occasional presence of a tumour having the structure of the thyroid gland in the position of the foramen cæcum, and to remind our readers that such a "tumour" may be associated with absence of the normal gland.

Sarcoma of bone is undoubtedly the most important example of this form of malignant disease. The malignancy of bone sarcomas, excluding the myelomas or "myeloid sarcomas" which are now by most observers recognized as benign growths, is extremely high. Indeed no more malignant affection can be imagined than a periosteal *sarcoma of the shaft* of the femur in a young subject. Probably no part of the skeleton is exempt, but in considering the most important features of sarcoma of the bones it will be convenient to restrict our remarks chiefly to the long bones of the limbs, in which the disease is most common.

Sarcoma of the **long bones** occurs in two forms—the central or endosteal, and the periosteal. Of these the latter is by far the more common, the difference being probably much greater than most

statistics on the subject suggest, because of the inclusion in these statistics of myelomas among the central sarcomas. Both forms tend to arise in the articular extremity rather than in the shaft. This

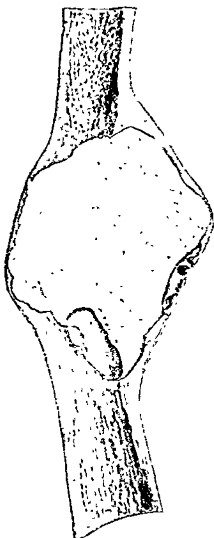


Fig. 122.—Endosteal fibro-sarcoma of shaft of femur in longitudinal section.

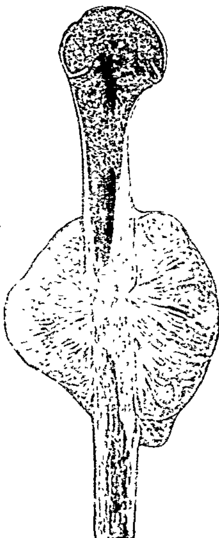


Fig. 123.—Periosteal fibro-sarcoma of shaft of humerus in longitudinal section.

is especially true of the endosteal tumours, which are exceedingly rare except at the extremity.

A *central sarcoma*, as it increases in size, causes "expansion" of the compact wall of the bone (Fig. 122), which usually becomes pro-

gressively thinned until at one or more spots the bony shell becomes completely destroyed and the tumour substance projects beneath the periosteum and in its further growth behaves like a tumour beginning in this situation. Even without any macroscopic defect in the bone, a central sarcoma may reach the exterior by way of the vascular

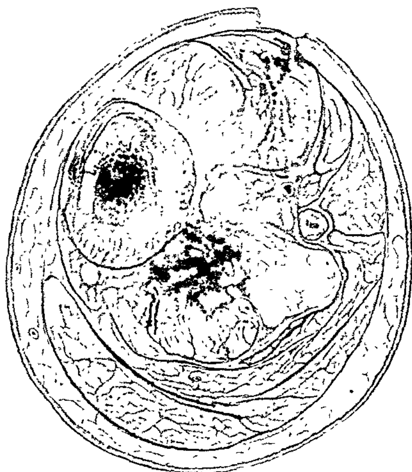


Fig. 124.—Section of leg showing a subperiosteal sarcoma of the tibia. (University College Hospital Museum.)

channels in the osseous tissue. The extent to which a bone may be expanded by a central sarcoma is illustrated by the macerated specimens to be found in all pathological museums. The process is, of course, not a mechanical one. While the osseous tissue is destroyed from within by the growth of the tumour, fresh periosteal bone is being deposited externally, and thus, especially in the earlier stages, the bone may become thicker, and not thinner, as it is undergoing

expansion. A central sarcoma often extends along the medullary canal far beyond the limits of the enlarged part of the bone.

A *periosteal sarcoma*, especially when affecting the shaft, tends to spread around the whole circumference of the bone, sometimes without causing more than slight erosion of its surface. The tumour usually assumes a more or less globular and somewhat lobulated form (Fig. 123), and although the neighbouring muscles are intimately incorporated with its surface the line of demarcation between the two is well defined (Fig. 124). Just as a central sarcoma tends to grow through the osseous tissue, so a subperiosteal sarcoma tends to invade the medullary canal As a result of the weakening of the bone, spontaneous fracture is not an uncommon occurrence (Fig. 125), but is less frequent than in secondary carcinoma It is most likely to occur *when the tumour involves the middle part* of the shaft. Sarcomas, although particularly prone to begin at the extremities of the long bones, rarely actually involve the joint cavity, and, as in the case of the myelomas, the articular cartilage usually remains intact, even though the tumour substance extends to its deep *surface*

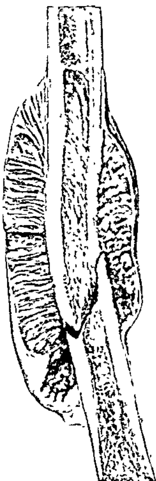


Fig. 125. — Spindle-cell sarcoma of periosteum of shaft of femur, leading to spontaneous fracture.

(*This and the three preceding figures are from specimens in the Museum of University College Hospital*)

The clinical distinction between a central and a periosteal sarcoma can often be made with tolerable certainty, even without X-ray examination. In the former, although the tumour may project only from one aspect of the bone, it can generally be detected that the bone is *enlarged in other parts of its circumference*. The periosteal tumour is likely to be more extensive; it projects as a somewhat lobulated mass from the bone, often surrounding its whole circumference, and the borders of the tumour in relation to the bone are more abrupt. It is also of importance that pulsation can more often be detected in a central growth, in that part which has projected through the *expanded osseous tissue*.

Among the most important varieties of sarcoma which affect the bones are round-, spindle-, and mixed-cell sarcomas, angio-sarcoma (endothelial sarcoma), chondrifying sarcoma, and ossifying sarcoma. Probably the most common form of periosteal sarcoma is the spindle-cell, and it is in this form that chondrification and ossification are most commonly seen. Round-cell sarcoma is said to occur more frequently as a central growth.

The formation of cartilage or bone in a sarcoma of bone may be so slight as only to be detected on minute examination, or, on the other hand, may be so marked a feature of the tumour as to give it the appearance of a mass of cartilage or bone. Microscopical examination may alone enable the true nature of the tumour to be determined (pp. 512–13). If an ossifying sarcoma is macerated, it is often found that the bone in the tumour presents the form of long, closely packed spicules radiating from the surface of the bone.

The development of a sarcoma in a bone at the site of a previous fracture may be mentioned as a rare occurrence. In this connexion it is obviously very important not to confuse the sequence of events, for, as we have seen, fracture resulting from a sarcoma is not uncommon. Cases in which such a mistake may safely be excluded are recorded, as, for instance, that described by Shattock, in which a chondrifying sarcoma of the humerus first showed itself about twelve weeks after a traumatic fracture which had repaired normally. Amputation was performed at the shoulder-joint, and death occurred about two years later with symptoms of recurrence in the chest.

Reference may also be made to other pathological conditions following fractures, which may be mistaken for a malignant growth. Among these are, first, cases in which from various causes an exaggerated formation of callus occurs; secondly, diffuse osteoma as recorded by Battle and Shattock; and, lastly, a condition illustrated by a remarkable case brought by Bilton Pollard before the Pathological Society of London, in which, following an injury to a child's leg, not certainly a fracture, there was an enlargement of the tibia and fibula which was treated by amputation. In this case the tumours, which were regarded clinically as sarcomas, were after removal considered to be due to simple hypertrophy of callus, but more recent examination of the specimen by Shattock seems to make it probable that the spongy, bony tumours were inflammatory, and examples of the rare condition for which the name "non-calcifying plastic osteitis" or "fibrous osteitis" is applied. It will thus be [illegible] much consideration is necessary before [illegible]ing that a [illegible] a bone following a fracture is sar[illegible]d requires a[illegible]

Among th[illegible] of the limbs[illegible], and humerus are the most l[illegible]. prob[illegible] giv[illegible] and in

these bones the upper ends of the tibia and humerus and the lower end of the femur are the favourite sites. The radius and fibula are rarely, and the ulna very rarely, affected. Invasion of the lymphatic glands is exceptional, but is probably less rare in the round-cell than in the spindle-cell growths. The extreme malignancy of bone sarcoma is manifested chiefly by the tendency of the disease to cause metastases, especially in the lungs, and the relative malignancy in different cases seems to be determined rather by the particular bone which is affected and by the central or periosteal origin of the growth than by differences in microscopic structure. Thus, although in general terms round-cell sarcoma is more malignant than spindle-cell, this statement can hardly be applied to sarcoma of the long bones, because periosteal tumours, although usually composed of spindle cells, are so intensely malignant. The presence of a pronounced tendency to ossification or chondrification might also on general grounds be expected to diminish the malignancy of a bone sarcoma, but most surgeons will agree with Butlin that this is not so. An extensively ossified or chondrified spindle-cell sarcoma of the periosteum appears to pursue a course as malignant as that of a similar tumour in which no such specialized tissue is present. In these cases also, as already pointed out, it may be found that the metastases in the lungs show a correspondingly mixed structure.

In connexion with the symptoms produced by a sarcoma of bone, it may be said that in the early stages they are in no way characteristic. After a fixed pain in the part, lasting probably several weeks or a few months, often referred to the neighbouring joint and wrongly attributed to rheumatism, a swelling is noticed, which may also closely simulate an enlarged joint.

The symptoms, as regards both pain and swelling, are usually continuously progressive, and thus are often in striking contrast with those due to inflammatory conditions in which more or less marked intermissions are common. The amount of interference with the movements of the neighbouring joint is usually less in the case of a bone tumour than a bone inflammation.

It occasionally happens that spontaneous fracture results from a sarcoma of the bone before the other symptoms are at all pronounced. Thus, in the case of a man aged 35, who was under the care of Christopher Heath, slight pain and swelling had been noticed in the right arm for five months, when the limb suddenly fell helpless whilst being raised to box a boy's ears, spontaneous fracture having occurred at the seat of a periosteal spindle-cell sarcoma of the humerus.

Enough has been said to show that the early diagnosis of a sarcoma of one of the long bones may be attended with great difficulty.

1. At the risk of repetition, it may be pointed out that the differentiation from various *inflammatory conditions* may be particularly difficult, especially from such conditions as syphilitic periostitis and osteitis, tuberculous osteitis, and central chronic abscess. In this connexion X-ray examination will prove of the greatest value.

The most striking features of the radiograms obtained in the chief conditions which may simulate a sarcoma of bone may be stated as follows: In a localized enlargement due to chronic periostitis with superficial osseous deposit the radiogram is characterized by the presence of lines parallel to the surface. In a central abscess with surrounding sclerosis the enlarged part of the bone gives a dense shadow in which is a paler area, sometimes surrounding the denser shadow of a sequestrum. In a tuberculous bone, Shenton states that "instead of the clear outline of the bones and their cancellated structure, a fluffy effect is seen, the outline being blurred and the cancellous tissue difficult of detection." Shenton further points out that the bone around a tuberculous cavity is poor in mineral matter, and, being more transparent than usual, the contrast between it and the abscess cavity may be very slight. In a central tumour, such as a myeloma, the expansion of the bone may be very obvious; whilst in a periosteal sarcoma there may be very marked irregularities about the affected part of the bone, and in the tumour itself ossification or calcification may produce an irregular spotted appearance quite unlike the linear arrangement of the new bone in periostitis. If other means fail, no time should be lost in establishing the diagnosis by means of an exploratory incision. (*See also* p. 665.)

2. From *chronic articular disease* a sarcoma in the joint extremity of a long bone can usually be distinguished by careful examination, and the same considerations must be taken into account as were mentioned in connexion with the diagnosis of myeloma (p. 433).

3. The diagnosis from *sarcoma of the soft structures*, such as the muscles, is not usually difficult, except in advanced cases when such a tumour has contracted secondary attachments to the bone.

4. A periosteal sarcoma sometimes increases rapidly in size as the result of hæmorrhage into its substance. This may cause a close resemblance to a *chronic abscess*, and in the same connexion it may be mentioned that especially in infants a *periosteal hæmorrhage* may simulate a new growth.

5. The pulsation in a vascular sarcoma protruding from the expanded bone has occasionally produced a close resemblance to an *aneurysm* of the adjacent large artery.

6. It cannot be too strongly insisted that in every case of suspected sarcoma of bone in a middle-aged or elderly subject the possi-

bility that the tumour is a *secondary carcinoma* must be carefully considered (p 554).

The only available **treatment** in most cases of sarcoma of the long bones is amputation, and when the growth is periosteal the whole bone should be removed. Exception may, perhaps, be made in certain cases in which the tumour is situated at the extreme lower end of the femur, when amputation may be performed below the trochanters rather than at the hip-joint. In those very rare cases in which sarcoma affects the fibula or one of the forearm bones it may sometimes be justifiable to practise a free removal of the affected part of the bone in place of amputation.

The **prognosis** in periosteal sarcoma of the long bones, even after high amputation in early cases, is most unfavourable. Of 68 cases of periosteal sarcoma collected by Butlin in 1900, there was only one in which a cure seems to have been effected, the patient being alive and well eight years after the operation, and even in this case there is some doubt whether the tumour was not central in origin. Much further evidence as to the extreme malignancy of periosteal sarcoma of the long bones was brought forward in the discussion at the Royal Society of Medicine in 1912. Thus, in 25 consecutive cases of periosteal sarcoma of the femur treated at St. Bartholomew's Hospital, none of the patients was alive three years later.

Of sarcomas of **other bones** little more need be said than that they may occur in any situation, such as the skull, spine, sternum and ribs, scapula, clavicle, pelvis, patella, and in the bones of the hand and foot. In some of these situations the early diagnosis may be most obscure, and the most various symptoms, such as those due to pressure on the spinal cord when the spine is involved, or on the sciatic nerve by a tumour of the pelvis, may precede the detection of a tumour. Even in readily accessible situations the difficulty in early diagnosis may be great, as, for instance, in a case of round-cell sarcoma of the os calcis, in which the disease was at first regarded and treated as tuberculous, until the detection of pulsation, as the swelling increased, revealed its true nature.

Sarcoma of the **jaws** is not uncommon, and is most frequently periosteal in origin. The term "central" as applied to tumours of the maxilla is liable to be misleading if used for all tumours arising in the antrum, for probably such tumours, as a rule, arise in the muco-periosteum lining the cavity. Sarcoma is more common in the mandible than the maxilla, and all the forms already described in the long bones may occur in this situation. Sarcoma of the maxillary antrum is very malignant, and may extend very insidiously to the surrounding cavities.

Sarcoma of the alimentary canal may occur at any part of its length, and probably arises most commonly in the

mucous membrane or the submucous tissue, or beneath the serous coat. In a communication on this subject made by Corner and Fairbank to the Pathological Society of London in 1905, 175 cases are tabulated, and show the following distribution, viz.: œsophagus, 14; stomach, 58; small intestine, 65; ileo-cæcal region, 20; large intestine, 11; and rectum, 7. In the small intestine the disease increases in frequency in passing from the duodenum to the ileum.

In the submucous variety the tumour may assume an annular form, or may project into the lumen as a polypoid mass. In the subserous form, as in the stomach, a large pedunculated tumour may result.

The round-cell form is most common, and glandular invasion is present in about one-third of the cases. Metastases in the lungs appear to be rare, but are common in the liver and kidneys. In the intestine intussusception may result and cause hæmorrhage, but, apart from this, hæmorrhage is rare. Melanotic sarcoma has several times been recorded in the lower part of the rectum.

Among the features which may help to distinguish sarcoma of the alimentary canal from carcinoma, Corner and Fairbank mention the rapid course of the disease and the early occurrence of marked anæmia and wasting, the presence of a tumour of considerable size, the absence of hæmorrhage, and the presence of irregular fever.

Sarcoma of serous membranes usually occurs in the form of an endothelial sarcoma. Such a growth may be illustrated by certain tumours of the pleura which may take the form of a diffuse thickening of the serous membrane, associated with the presence of nodules on the surface, and of infiltrating masses of growth extending into the mediastinal tissues and the substance of the lung. In one case of this kind a mass of growth extended from the apex of the lung into the tissues at the root of the neck.

In the peritoneum similar growths have been met with and may have the diffuse characters above described. The recognition of this form of sarcoma may be attended with much practical difficulty. Thus, it may closely resemble a chronic inflammatory thickening of the peritoneum, or a diffuse carcinomatous infiltration secondary to a primary carcinoma, especially of the stomach.

In the cerebral and spinal meninges sarcoma may occur as an angio-sarcoma, in which the peculiar hyaline degeneration of the vessels already mentioned may be present (p. 526). Sarcomas of the meninges may extend into the brain substance, or perforate the skull.

Sarcomas occasionally arise in the **subserous tissue**, especially of the peritoneum. Retroperitoneal sarcoma usually occurs as the round-cell form, and in some instances arises in the aortic glands as a lympho-sarcoma. In other cases the growth probably begins

in the perirenal connective tissue. Tumours of this nature often reach large proportions, and may readily be confused with other abdominal growths, especially of the kidney. Subserous sarcomas are occasionally met with in the omentum and mesentery. Similar tumours also occur in the mediastinum.

Sarcoma of the kidney.—*In adult life* sarcoma of the kidney is rare, and probably usually takes its origin in connexion with the renal capsule; indeed, many tumours having clinical features *suggesting a renal origin arise in the perirenal tissue, and are to be* regarded as retroperitoneal sarcomas. At all ages it is necessary to distinguish clearly between the renal sarcomas and renal hypernephromas.

In early life a tumour of the kidney is not uncommon which is known by the names of renal sarcoma of infants, adeno-sarcoma, myosarcoma, and embryonic tumour. It is characterized by the enormous size which it may rapidly attain, often without hæmaturia or pain

Examination of such a growth shows that it is usually soft and lobulated, yellowish-white in colour, and sometimes cystic, and further that it does not appear to originate in the kidney substance itself but in the neighbourhood of the hilum, and that as it increases in size it displaces the kidney substance, so that the latter may eventually form a thin layer spread out over the surface of the growth. Not very infrequently the tumour is bilateral.

Microscopically the structure of tumours of this class differs widely, sometimes in different parts of the same growth. In some instances the structure appears to be that of a simple round-cell sarcoma, whilst in others the most striking histological feature is the presence of spaces or branching tubules lined with cubical or columnar cells, as in Fig 126. On account of this structure the name adeno-sarcoma is sometimes applied to the tumours of this class According to Nicholson, who discusses the subject fully in *Guy's Hospital Reports*, tubules can always be found on careful examination of tumours which at first sight appear to be pure round-cell sarcomas. In the trabeculæ which separate the cellular masses, plain muscle-fibres are often present, and occasionally striated muscle, cartilage, and other structures have been demonstrated.

Although for convenience we have described this form of renal tumour among the sarcomas—and indeed in many instances the tumour has for the most part a sarcomatous structure—it is clear from the above description that the growths in question are of a composite nature. The complicated structure can probably be most satisfactorily explained by supposing that the tumour has arisen in tissue derived from an undifferentiated portion or "rest" of a mesoblastic segment.

The lymphatic glands are not infrequently the seat of secondary deposits, and metastases are most common in the lungs and liver.

The *prognosis* after removal of tumours of this nature is very unfavourable. The mortality resulting from the operation is still high, and very few cases of prolonged freedom from recurrence are on record.

Sarcoma of the testicle is not common, and in many recorded cases seems to have been very definitely related to a previous



Fig. 126.—*Microscopic section of embryonic tumour of kidney of a child.*

injury. It is usually of the small round-cell form. Both clinically and histologically it closely resembles the soft, spheroidal-cell form of carcinoma which chiefly affects this organ. Nicholson, who has written a valuable thesis on new growths of the testicle (*Guy's Hospital Reports*), is of opinion that many soft cancers have been classed as sarcomas, and that sarcoma is really the less common of the two forms of malignant growth. The tumour presents itself as a uniform enlargement of the testicle, often so soft and elastic as to be confused with a fluid swelling. In the later stages it may perforate the coverings of the testicle, and even fungate through the scrotum. Sarcoma of the testicle in young children may be bilateral.

The tendency of sarcoma of the testicle to cause metastases by way of the lymphatics as well as the blood-stream is generally regarded as greater than in the case of sarcoma in most other situations, but, as Nicholson suggests, this tendency is probably less pronounced than is generally supposed, on account of the confusion between sarcoma and soft cancers. The glands first involved are those which lie on either side and in front of the aorta and vena cava, between the level of the renal vessels above and the bifurcation of the aorta below.

The secondary glandular deposit may reach a large size and form a prominent tumour situated chiefly above the level of the umbilicus. Enlargement of the inguinal glands is very unlikely to occur unless the disease of the testicle has involved the scrotum, but it is of interest that enlargement of the left supraclavicular glands has been observed (p. 492).

Sarcoma and the other forms of new growth affecting the testicle may develop in an organ which is retained in the inguinal canal or abdominal cavity, and it is generally supposed that malposition of the testicle renders it more than usually liable to malignant disease. On the other hand, we have records of two cases in which the malignant disease occurred in the normally placed testicle, the opposite one being retained. The much greater frequency of inguinal than of abdominal retention explains the greater frequency of malignant growths in the former situation. When a testicle in the abdomen is affected, a tumour situated laterally below the level of the umbilicus is produced, the nature of which may be altogether obscure until the absence of the corresponding testicle from the scrotum is observed. Osler, who has drawn attention to the clinical characters of the tumours resulting from malignant disease of an abdominal testicle, has found that ascites is not uncommon.

Although attempts have been made to apply to malignant disease of the testicle the general principle of extirpating the corresponding lymphatic area, Jamieson and Dobson, as the result of their investigations on the distribution of the glands receiving the lymphatics of the organ, doubt whether such an object is attainable.

Sarcoma of the ovary in adults is usually bilateral, and may reach a large size, tending to spread to the surrounding structures and to cause metastases. The characters of the tumour itself are liable to vary according as it is round-celled or spindle-celled, the former being much the softer of the two.

In connexion with the not infrequent occurrence of sarcoma of the ovaries in young children, it may be convenient here to refer to the fact that sarcoma is known to affect **the other pelvic organs in young children**, such as the prostate, testicles, uterus, vagina, and bladder. In the ovaries and testicles the disease is not uncommonly bilateral. In

the bladder, sarcoma in children may occur as a fungating mass, but more often assumes a polypoid form in which the sarcoma elements are largely mixed with myxomatous tissue. Targett, who studied tumours of this nature, was of opinion that most cases described as *mucous polypi* of the bladder in children are really sarcomatous. The tumour may reach a large size and prove fatal by obstruction of the ureters. In the uterus and vagina, sarcoma in early life may also assume a similar myxomatous and polypoid form, and the disease is likely to involve the bladder wall and eventually extend into the interior of the viscus in forms similar to those of the primary vesical growths. Among 26 cases of sarcoma of the vagina in children, collected by D'Arcy Power, the wall of the bladder was involved in 10 Sarcoma of the prostate is also not very rare in early life, and, like the similar tumours beginning in the other pelvic viscera, may form a tumour of large size projecting upwards above the pubes.

Sarcomas of these organs in children thus form a definite group characterized by the tendency of the growth to become polypoid and myxomatous. The disease appears usually to originate in the submucous tissue, although in the case of the prostate the growth may probably begin in the fibrous capsule of the gland, and in some tumours the origin appears to be rather in the pelvic cellular tissue than in the viscera themselves.

Further reference is hardly necessary to primary sarcoma of the bladder, prostate, and vagina in adults, the disease not being common in any of these situations.

In the adult **uterus** sarcoma may occur in several forms. In one variety it appears as a fungating mass projecting into the uterine cavity and tending to become polypoid, and even extending into the vagina, whilst in other cases the tumour extensively infiltrates the uterine wall and may extend through its whole thickness so as to form nodular projections beneath the peritoneum. Sarcoma of the uterus may also occur as a malignant transformation of a fibro-myoma. To the naked eye the change may not be striking, but sometimes the characteristic appearance of the simple tumour gives place to a more homogeneous and waxy appearance. Microscopically the elongated muscle cells are found to be separated by sarcoma cells—oval, spindle-shaped, or multinucleated.

A rare variety of sarcoma of the uterus is the grape-like form in which the cervix is distended by polypoid masses that may project into the vagina and even infiltrate its wall. This form corresponds with that sometimes occurring in young children, which has been already mentioned.

True **sarcoma of the breast** is rare, and statistical statements on the subject have in the past been rendered to a large extent

valueless by the inclusion among the sarcomas of those softer, more rapidly growing forms of fibro-adenoma under the name of adeno-sarcoma. The name must be reserved for malignant connective-tissue tumours in the growth of which the glandular elements take no part.

A sarcoma of the mamma shows for a considerable time a striking tendency to encapsulation, a definite fibrous layer intervening between the tumour substance and the surrounding tissues. The spindle-cell variety is the most common, but round-cell sarcoma, alveolar sarcoma, and myxo-sarcoma also occur, and in rare instances true cartilage has been present in the tumour. In the softer forms, hæmorrhagic extravasations and cystic changes are common. The tumour presents clinical features which are in many respects intermediate between a soft fibro-adenoma on the one hand and a soft carcinoma on the other. Thus, although not presenting the free independent mobility of a fibro-adenoma, it does not attach itself to the surrounding structures so early as a carcinoma. Glandular enlargement may be absent even in the later stages. The tumour, if allowed to continue its growth, may reach a very large size, and eventually will fungate through the skin in the manner already described (p. 522). The diagnosis of the disease from various cystic conditions and from the other soft, solid tumours of the breast is beset with difficulty, but excision of the suspected tumour will usually enable the surgeon to decide whether or not to proceed at once to the complete operation on the same lines as those adopted for carcinoma. Dissemination by way of the blood-stream may occur, but in some cases of sarcoma of the breast the malignancy is chiefly manifested by local recurrence after operation, the recurrences being sometimes spread over a period of many years.

Sarcoma of the thyroid gland is probably less common than carcinoma, and is usually of the simple round- or spindle-cell variety. It can hardly be distinguished clinically from soft carcinoma, although Berry points out that ordinarily it is of more rapid growth and shows a greater tendency to be limited to one lobe. The invasion of the surrounding structures, especially the trachea and lymphatic glands, soon renders the disease inoperable.

Sarcoma of the brain is much less common than glioma, but may occur as the round- or spindle-cell form, or as a glio-sarcoma. A sarcoma of the brain substance may be indistinguishable with the naked eye from a glioma, but differs from it in its tendency to involve the membranes, and even the bone.

Sarcoma of nerves.—Sarcoma of the large nerve-trunks is very rare, and has been met with chiefly in the lower limbs, the sciatic nerve being most commonly affected. Among the recorded

cases the spindle-cell form has been the most frequent, but round-cell sarcoma and myxo-sarcoma have been met with The tumour caused by a sarcoma of a large nerve-trunk may attain a large size; it tends to become lemon-shaped as the result of the extension of the growth for a short distance into the nerve-trunk at each pole of the tumour. The nerve-fibres themselves are more or less extensively destroyed by the infiltrating growth, and the function of the nerve correspondingly interfered with. In this respect the sarcoma contrasts with a simple tumour of a nerve-trunk.

From a study of recorded cases, Alexis Thomson finds that the malignancy of sarcoma of the nerve-trunk of the limbs is very high, and that even after removal of a considerable part of the affected nerve-trunk, together with the tumour, local recurrence, followed by metastases, has usually occurred. High amputation should, when practicable, be practised as early as possible.

Reference has already been made to the supervention of sarcoma in cases of neuro-fibromatosis (p. 406).

Sarcoma of the eye occurs as an intra- or extra-ocular growth, the former being the more common. Intra-ocular sarcoma affects some part of the uveal tract. It is relatively rare, the choroid being most frequently affected, the ciliary body less frequently, and the iris very rarely. It is always primary, never multiple, and generally pigmented (melanotic sarcoma). In the choroid it grows inwards and raises the retina, which ultimately becomes completely detached. If the eye is not removed, secondary glaucoma occurs, and the growth extends outside the globe along the perforating vessels Metastatic deposits are formed first in the liver. The cells vary greatly in different cases, but are usually spindle-shaped, and the growths are very vascular

Epibulbar sarcoma is rare, occurring in the conjunctiva, and springing usually from the neighbourhood of the caruncle, especially from the plica semilunaris. Probably it generally originates in a congenital mole.

CARCINOMA

A carcinoma is a malignant tumour arising in epithelium and characterized by a progressive invasion of the adjacent tissues by the epithelial cells. The only essential constituent of a carcinoma is the epithelium, while the stroma, which often forms a considerable part of the bulk of the tumour, is merely an expression of the reaction of the tissues to the infiltrating epithelial growth. The stroma is, therefore, absent at the spreading edge of the tumour where the earliest invasion of the tissues by the advancing epithelial cell-columns is taking place. Again, when the lymphatics of a part are permeated by cancerous

epithelium, the stroma reaction may be absent, and the recognition of the nature of the disease depends entirely upon the abnormal presence of epithelial cells in the part. Further, in the rare form of malignant epithelial tumour known as chorion-epithelioma, the epithelial elements, being largely intravenous, do not occasion any stroma reaction.

When, however, as is usually the case, a well-marked stroma reaction occurs, the carcinomatous tumour assumes the *alveolar arrangement* which is seen when a section is examined microscopically.



Fig. 127.—Microscopic section of spheroidal- or polyhedral-cell carcinoma of the breast.

The irregularly branching epithelial columns or tubes, being cut across in different relations to their length, appear as separate cell areas occupying spaces in the stroma. The *stroma* varies greatly both in character and amount, and takes an important share in modifying the characters of the tumour. In some instances it merely forms slender strands carrying blood-vessels between the masses of cancer cells, whilst in others it constitutes the bulk of the growth, and the masses of epithelial cells are few and small. In its character, also, it presents striking variations, consisting sometimes of dense fibrous tissue with scanty cell-elements, and at other times of richly cellular

vascular tissue, almost like granulation tissue in appearance. varying proportion of the epithelial elements and stroma, and variat in the character of the latter, *explain the differences* noticed in consistence of carcinomatous tumours, these differences being pronounced that while some growths are extremely dense and h others are soft and almost brain-like.

From what has been said it will be evident that the fundame criterion upon which the recognition of a carcinoma depends is



Fig. 128.—Microscopic section of spheroidal- or polyhedral-cell carcinoma of the breast.

epithelial nature of the essential cell-elements. This can only occasionally be proved by tracing a direct continuity between the tumour cells and a surface or glandular epithelium, but, even when this is not possible, valuable evidence may be obtained by noticing that the cells lie in immediate contact, or are merely separated by an almost imperceptible amount of intercellular substance, and that no extensions of the stroma or blood-vessels penetrate into the cell-masses (Figs. 127, 128). The line of demarcation, too, between the cell-masses and

the surrounding stroma or other tissues is very sharply defined, especially when, as in specimens treated with fixing reagents, the masses of cells shrink away from the tissue surrounding them (Fig. 127).

As cancer always arises in epithelium, it is not surprising that the irregularly proliferating cells of the new growth retain in vary-



Fig. 129.—Microscopic section of squamous-cell carcinoma of skin.

ing degree the morphological characters of the particular form of epithelial cell in which the growth originated, and thus the spheroidal- or polyhedral-cell, the squamous-cell and the columnar-cell varieties of carcinoma are recognized. Of these forms the spheroidal- or polyhedral-cell variety, such as occurs in carcinoma of the breast, is the most undifferentiated. On the other hand, carcinomas originating in squamous or columnar epithelium may retain a highly differ-

entiated form, so that the character of the cells in which the tumour *originated can be clearly recognized.* Such, however, is not always the case, but the cell-masses of a carcinoma arising in a columnar or stratified epithelium may in the course of their growth become indistinguishable from those arising in the spheroidal or polyhedral cells of a glandular organ.

In **spheroidal- or polyhedral-cell carcinoma** the *cells* are arranged in solid masses (Fig 127), they vary much in form,



Fig. 130.—Microscopic section of squamous-cell carcinoma of skin.

and whilst in some tumours or parts of tumours they are spheroidal, in others they lose their spheroidal shape, chiefly as the result of the pressure of adjacent cells one upon another, and become altogether irregular, flattened, or polyhedral (Fig. 128). The individual cells usually possess an abundant granular protoplasm, and a large round

or oval nucleus, in which considerable variations in the amount of chromatin will often be noticed.

Squamous-cell carcinoma originates in a stratified or transitional epithelium, and when it retains its typical form is characterized by the presence of prickle-cells and the tendency of the cells to undergo horny change. The prickle-cells resemble those normally present in the stratum mucosum of the skin. The horny change or keratinization occurs in the central cells of the epithelium-columns, which, being farthest removed from the stroma, correspond to the most superficial layers of a stratified epithelium. As a result, the well known *cell-nests* or epithelial pearls are formed in the cell-columns On section, they present a characteristic concentric striation due to the presence of layers of horny scales in the centre (Figs. 129, 130).

It will thus be seen that in a typical squamous-cell carcinoma the cells of the epithelial columns present, when traced from the periphery to the centre, similar changes to those seen in the normal stratified epithelium

Columnar-cell carcinoma originates in the columnar epithelium covering a surface or lining a duct, and in its most typical form the shape and arrangement of the normal epithelium may be so completely reproduced that in place of solid cell-columns the cell-elements are arranged in a single layer of columnar or cubical cells around a central lumen (Figs 131, 145). It cannot be too clearly recognized that although carcinoma arising in stratified or columnar epithelium may retain the highly differentiated form of cells, this is not always the case. The tumour cells may revert to a more undifferentiated form, so that the character of the epithelium from which the growth originated may not be traceable, and the growth must be described as a spheroidal- or polyhedral-cell carcinoma.

Occasionally, still more specialized forms of carcinoma are met with in which the normal characters of the cells, functional as well as morphological, are strikingly preserved. For instance, in one form of cancer of the thyroid the tumour cells closely resemble those of the normal gland, secreting colloid substance, and even serving a useful purpose in metabolism, as shown by a case of von Eiselsberg's, quoted by von Bergmann In this case the symptoms of postoperative myxœdema, following the removal of a cancerous thyroid, subsided as a secondary tumour developed in the sternum, and the subsequent removal of the secondary growth was followed by tetany and death. Further evidences of the fact that cancer cells may retain in some degree the function of their normal epithelial antecedents is afforded by the presence of mucus-containing goblet cells in columnar-cell carcinomas, and the demonstration of glycogen in the cells of cancer

of the liver and of special ferments in cancers of the stomach and pancreas.

Secondary changes.—Carcinomas, more especially of the soft cellular forms, are liable to **fatty degeneration** and necrotic softening, which may be so slight as merely to produce yellow granular areas in the tumour substance, or may be so extensive as to cause liquefaction of a considerable part of the growth. The degeneration of the tumour substance may also be occasioned by extravasation of



Fig. 131.—Microscopic section of columnar-cell carcinoma of sigmoid colon. The distinction between the normal glands and the alveoli of the tumour is well marked.

blood, but, on account of the difference in the vascular arrangement, this is less common than in the sarcomas. Occasionally the structure of a carcinoma is very extensively modified by a **colloid** or **mucoid degeneration** of the cancer cells. This will most conveniently be considered in connexion with carcinomas of the breast and alimentary canal, in which it is most frequent. In carcinomas of superficial origin, as well as in those which, beginning deeply, have invaded a cutaneous or mucous surface, **ulceration** is very common, and the

ulcer often assumes characters which clearly show that it has resulted from a malignant growth. The surface of the ulcer is usually irregular, deep furrows or excavations being surrounded by prominent firm pink nodular masses looking like exuberant granulation tissue and often bleeding readily when touched. The edges of the ulcer are raised and nodular, and frequently everted or even overhanging, and the margin of the undestroyed skin or mucous membrane often ends abruptly at the edge of the ulcerated surface. The indurated base of the ulcer is formed by the deeper part of the growth extending into the subcutaneous or submucous tissue, and in the case of a small

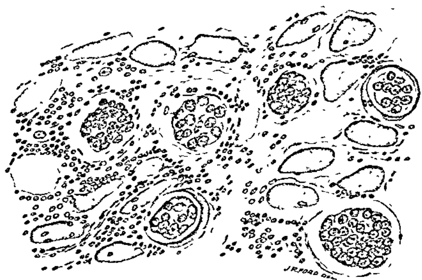


Fig. 132.—Microscopic section of muscle, showing invasion by carcinoma. From a carcinoma of the breast invading the pectoralis major.

superficially ulcerated carcinoma, as, for instance, on the lip, is a feature of great diagnostic value. The discharge from an ulcerated carcinoma usually consists of a thin blood-stained fluid, often with a peculiarly offensive odour.

In many circumstances, especially in carcinomas of the alimentary canal, secondary suppuration takes place around the ulcerated tumour, and thus the malignant nature of the disease may be entirely masked. For instance, in carcinoma of the cæcum a large pericæcal abscess may result, which may readily be mistaken for suppurative appendicitis.

The macroscopic appearances and clinical features of the varieties of carcinoma differ so widely that it is impossible to give any general

description of the disease, and the most important examples will be described as they occur in different situations.

Extension of carcinoma.—The intimate relation existing between the cells of a carcinoma and the lymphatics has already been considered, and if the spreading edge of such a tumour is examined,



Fig. 133.—Microscopic section of axillary lymphatic gland, the seat of a secondary deposit of *spheroidal-cell carcinoma. The* primary tumour was in the breast.

it is sometimes possible to demonstrate the presence of the lymphatic endothelium around the epithelial cell-mass (Fig 104, p. 487); but this is not always so, and there is no doubt that the cells of the infiltrating growth can advance in the tissues in a quite irregular manner. In Fig. 132 some of the groups of cancer cells are seen in the substance of the muscle-fibres. *The spread of the growth occurs by continuous extension,* and the apparently isolated cell-areas seen in a microscopic

section are really the cross sections of irregularly branching continuous columns or tubes.

The extension to the *lymphatic glands* occurs either by a process of embolism or by direct permeation of the intervening lymphatic vessels by the cancer cells (Fig. 133). In exceptional cases an indurated cord, caused by the infiltrated lymphatics, can be traced continuously from the primary tumour to the enlarged glands. In the latter the cancer cells are arrested in the lymph sinuses of the cortex; and it is a matter of much practical importance that the invasion of the glands does not at first cause a palpable enlargement, even though the glands are in a readily accessible position.

A lymphatic gland which is the seat of a secondary deposit of carcinoma presents in the early stages small, firm, white nodules of growth, chiefly in the cortex of the pinkish gland tissue. At a later stage, the whole gland may be greatly enlarged and infiltrated with growth having an appearance similar to that of the primary tumour. Finally, the growth may undergo extensive degeneration, breaking down into a thin milky fluid.

Clinically, the glands, even while still small in size, are usually characterized by their hardness, and as they enlarge they become adherent to the neighbouring glands and to the surrounding structures. Thus, in the glandular deposits in the neck consequent upon carcinoma of the tongue, the overlying sterno-mastoid becomes adherent to the glands and even invaded by the growth, while the large vessels, especially the internal jugular vein, may be so surrounded by the glandular mass that removal of the disease necessitates removal of part of the vessels also In advanced cases the glandular disease may involve the skin, and ulceration occur with the production of one or more openings through which the broken-down growth discharges, until, finally, a huge irregular cavity results, the profuse discharge, and often hæmorrhage, from which hastens the fatal result. In consequence of the septic condition of most carcinomatous ulcers of the skin and mucous membranes, a glandular enlargement in such cases may be the result of a simple lymphadenitis, and probably the marked tendency of the secondary glandular deposits in such cases to soften and break down may be partly due to the same cause.

The general subject of the **metastases** of malignant growths has already been considered, and it is unnecessary to refer again to the relative importance of the share taken by the lymphatics and blood-vessels respectively in the spread of the disease (p. 488) Little is known to explain the much greater liability of some parts than others to be the seat of metastases, and it is interesting to note that those parts which are most liable to primary cancer are rarely the seat of

secondary growths It is probable that very slight differences in the capillary circulation in different organs and tissues may be a not unimportant factor in determining their liability to metastases. This possibility has been considered by von Recklinghausen in connexion with the widely distributed bone deposits sometimes met with in certain forms of carcinoma, particularly of the thyroid, breast, and prostate. He suggests that the peculiar conditions of the circulation in the bones are very favourable to the arrest of cancer cells, and points out that the flow in the vessels of the medulla must at times tend to stagnate on account of the inability of the vessels in the osseous tissue to undergo changes in calibre.

A study of the different varieties of cancer, whether considered from the point of view of the structure or the position of the primary growth, reveals a striking difference in their liability to produce metastases. Many of the tumours having the structure of spheroidal-cell carcinoma exhibit a most striking tendency to cause secondary deposits in the bones and viscera, especially the liver and lungs. The squamous-cell and columnar-cell varieties, on the other hand, frequently prove fatal without any evidence of visceral or osseous deposits. For instance, a squamous-cell carcinoma of the tongue shows its malignancy by the progressive extension of the primary growth and an almost constant invasion of the lymphatic glands, whilst secondary deposits elsewhere are extremely rare. So, too, in carcinoma of the intestinal tract, often of the columnar-cell variety, metastases are very uncommon, with this notable exception, that the liver is often invaded by way of the portal circulation, and is the seat of multiple deposits As an instance of the very rare occurrence of bone metastases of columnar carcinoma, Bernard Pitts has recorded the case of a woman with carcinoma of the rectum upon whom colotomy had been performed ; spontaneous fracture of the humerus occurred, and on account of the excessive pain and the absence of union the limb was amputated The fracture had resulted from a deposit of typical columnar-cell carcinoma in the bone In a case in University College Hospital, under the care of Risien Russell, an unsuspected carcinoma in the upper part of the rectum of a man aged 32 caused metastases in the lumbar vertebræ, resulting in compression paraplegia, and also a deposit in the manubrium sterni.

We know of no explanation of the great variations in the tendency to produce metastases exhibited by the different forms of carcinoma. Although some of the most striking instances of widely distributed metastases are found in spheroidal-cell carcinoma, and some of the more differentiated forms exhibit the tendency in a much lower degree, exceptions are not uncommon Thus, the peculiarly special ized form of carcinoma sometimes occurring in the thyroid gland is

particularly liable to cause metastases, whilst in rodent ulcer, a carcinoma of a very undifferentiated type, the absence of secondary deposits is an almost constant feature.

In their structure the metastases of carcinoma reproduce in a very striking way that of the primary tumour in the character of the epithelial elements, and often any special degeneration, such as colloid, to which they may be liable. In view, however, of the fact that the stroma is not an essential part of the growth, but merely the result of a secondary reaction of the tissues it is not surprising that the

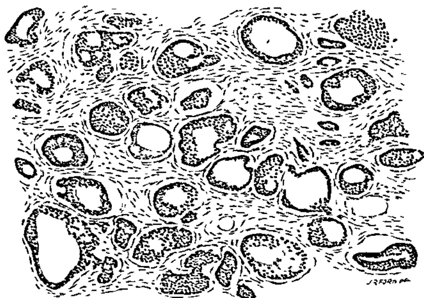


Fig. 134 —Microscopic section of secondary deposit of carcinoma in head of humerus. The primary growth was in the cervix uteri.

stroma of a secondary deposit may differ widely, both in character and amount, from that of the primary tumour. Thus, a small, hard cancer of the breast, in which the epithelial elements are very scanty, may produce large, soft metastatic deposits agreeing with the primary growth only in the character of the cells.

Secondary deposits of cancer in the bones are almost invariably central in origin and, especially when affecting the shaft of a long bone are very liable to occasion spontaneous fracture even before any enlargement of the bone can be detected. The presence of a fixed, dull aching pain in one of the bones of a patient suffering from carcinoma should always be viewed with suspicion. In rare cases the secondary invasion of the bones, instead of taking the form of

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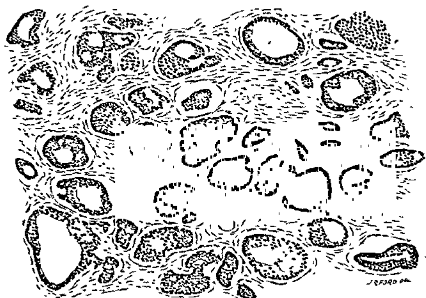


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localized deposits, occurs diffusely, and causes softening of the bones, resulting in deformity rather than actual fracture.

The subject of the metastases of carcinoma presents itself to the surgeon in two practical aspects. First, before deciding that a case of carcinoma is favourable for operation he must satisfy himself that no subjective or objective signs of metastases are present. Secondly, he must avoid the serious error of mistaking a secondary carcinoma for a primary tumour. This mistake is especially liable to be made in the case of bone metastases, and there can be no doubt that many limbs have been amputated for tumours supposed to be primary sarcomas, but which were carcinomas secondary to some unsuspected primary tumour perhaps altogether unproductive of symptoms. A woman aged 52 was admitted some years ago into University College Hospital for a swelling in the region of the right shoulder, which proved on examination to be a tumour of the humerus. It was regarded as a sarcoma, and amputation was performed at the shoulder-joint. Subsequent microscopic examination showed that the tumour was a carcinoma (Fig 134), and the patient was discovered to have an extensive cancer of the uterus.

Of especial interest in this connexion are certain cases of malignant *hypernephroma recorded by Albrecht and others, in which a single* bone deposit was the only metastasis. In a case of this nature recorded by Scudder of the Massachusetts General Hospital, a supposed sarcoma *of the upper end of the humerus proved, after amputation at the* shoulder-joint, to have the histological structure of an adrenal tumour. Attention was thus drawn to an indefinite tumour of the left renal *region, which proved to be a hypernephroma.* At the patient's death, nearly five years later, no other evidence of metastasis was discovered. In a similar case recorded by Pool, a pulsating tumour of the upper extremity of the fibula, also regarded before operation as a sarcoma, proved to be a secondary hypernephroma, and the patient, a man aged 57, subsequently showed signs of a rapidly growing tumour in the position of the right kidney. A consideration of such cases serves to [illegible] sarcoma of [illegible] subject, the [illegible] e tumour is secondary, and search for any evidence of a primary growth

Situation.—From what has been said, it is evident that a [illegible] which epithelium is present. [illegible] ıe most important characters [illegible] l organs.

Carcinoma of the skin occurs histologically in two forms, the squamous- and the basal-cell. The former is characterized by the presence of keratinized cell-nests and usually of more or less well-

marked prickle-cells. The basal-cell tumours, which originate in the Malpighian layer, are distinguished by the absence of cell-nests and prickle-cells, the cells comprising the cell-masses being undifferentiated in form, except the layer next the stroma, which is columnar. The basal-cell form of growth is most commonly associated with the *clinical features of rodent ulcer* (p. 562). *It will thus be seen that* the difference in structure of the two forms is associated with very considerable difference in malignancy.

Carcinoma of the skin affords some of the most striking examples of the relation of the disease to various forms of chronic irritation, ulceration and scarring, and, indeed, it is very rare for a cancer of the *skin to arise independently of some pre-existing pathological condition.* For this reason it is difficult to describe the earliest appearance of the tumour, which often begins as an apparently insignificant change in the characters of some simple ulcer or cicatrix. Two chief varieties may, however, be recognized—the warty form and the ulcerating form. In the **warty form** the surface of the growth presents a coarse, *irregularly papillary appearance, which may closely resemble that of* a simple papilloma, from which, however, it can usually be distinguished by the greater irregularity of the surface, and especially by the hard base upon which the papillary surface rests. The **ulcerating form** may, in its early stage, present no characteristic feature, but the indurated base is often noticeable, and as the ulcer extends it assumes *the typical characters of the carcinomatous ulcer already described* (p. 548)

A section through a squamous-cell carcinoma usually presents an opaque white colour and a coarsely granular surface; to the naked eye its outline is sharply defined, and the contrast between the nearly white tumour and the surrounding tissues is often very striking. *In all forms of carcinoma of the skin, except rodent ulcer, invasion of* the lymphatic glands usually occurs early, but apart from this the glands are often enlarged as the result of lymphadenitis due to infection from an ulcerated growth.

Some of the most extensive cases of cutaneous carcinoma are those in which the disease originates in **burn scars** on the limbs. In *such cases the new growth usually begins at the margin of the scar,* and often quickly involves a considerable area, assuming usually the warty rather than the ulcerating form. An interesting example of this form of the disease is the *kangri cancer* met with in Kashmir, caused by the basket of burning charcoal which the inhabitants of the cold hilly districts carry beneath their clothing. Neve, of the Kashmir Mission Hospital, found that *among* 1,189 *squamous carcinomas* removed during a period of twenty-five years, no less than 848 were examples of kangri cancer. The tumours usually occur

on those parts, the abdominal wall and inner aspects of the thighs, with which the kangri comes into contact, and the skin in which the disease arises usually shows marked evidences of the prolonged effects of heat in the presence of pigmentation, scarring, warty formations, or chronic eczema.

The most striking examples of the origin of cutaneous carcinoma in an **ulcer** are those in which it supervenes upon a chronic ulcer of the lower part of the leg. Here, as in scars, the edge of the ulcer is usually the starting-point of the growth, and in some cases the change may be so gradual that the patient may disregard it until the disease has extended deeply enough into the limb to occasion spontaneous fracture. In two instances of this kind which have come under our notice, the growth supervened upon an ulcer of the leg of thirty years' duration

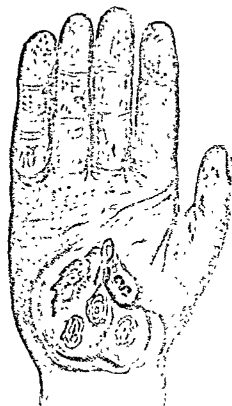


Fig. 135.—Carcinoma of palm supervening upon dermatitis resulting from prolonged administration of arsenic.

(*From the New Sydenham Society's Atlas of Pathology.*)

A carcinoma of the skin has occasionally been known to develop at the orifice of a **sinus**, such as may be due to chronic bone disease. In a specimen in the Museum of University College Hospital, an irregularly papillary carcinoma of the skin surrounds a sinus leading into an abscess cavity in the upper extremity of the tibia. There is no history to the specimen, but the discovery of a small fragment of lead in the wall of the cavity in the tibia suggests that the disease of the bone resulted from a bullet wound, and that the carcinoma arose at the orifice of a sinus which opened in the skin.

From the prolonged medicinal use of **arsenic**, usually in the treatment of psoriasis, the skin, especially of the palms and soles, may become dry, harsh, and so thickened as to produce a well-marked condition of keratosis, in which corn-like thickenings also occur. Hutchinson, who drew special attention to this subject, collected a

considerable number of cases in which carcinoma has supervened upon this condition, the malignant growth presenting itself as an intractable ulcer, beginning in a fissure or corn, usually on the hand or foot (Fig. 135). In one recorded case, a woman of 25, who since the age of 5 had frequently taken arsenic for pemphigus, and in whom the skin of the hands and fingers was very rough, developed a large ulcer, almost certainly malignant, behind the crest of the ilium, followed by a glandular swelling in the groin which ulcerated. This case is of special interest on account of the extreme rarity of carcinoma of the skin of the trunk.

Among 55 cases of squamous carcinoma of the skin of the hand, collected by Lenthal Cheatle, in 53 the disease occurred on the dorsum, and the most common site was found to be the skin covering the radial side of the second metacarpal bone. Two interesting observations have been made by Cheatle in connexion with this fact. First, in this position Head observed the formation of a trophic ulcer in an area rendered anæsthetic by division of certain sensory nerves, thus suggesting that this region is especially exposed to external irritation. Secondly, the atrophic changes sometimes met with in the skin in old age, in which it becomes shiny, smooth, inelastic, and pigmented, are especially pronounced in this situation.

A striking instance of the relation of chronic irritation to the development of cutaneous cancer is afforded by the occurrence of the disease in workers with pitch, tar, and paraffin. Legge, who has carefully investigated the subject, points out that in workers with anthracene and grease the arms and hands are chiefly affected, whilst in patent fuel briquette makers the scrotum is the most common seat of the disease. In a case which came under our notice the growth occurred on the dorsum of the hand of a labourer engaged in laying railway sleepers treated with tar. The changes which occur in the skin, and are liable to develop into carcinoma, are similar to those met with in chimney-sweep's cancer of the scrotum (p 593).

It has been found in the experimental production of tar-cancer of the skin in animals that sometimes the tumours disappear spontaneously, and in man much difficulty may arise in determining whether or not the lesions produced by tar and similar substances have actually become malignant.

Mechanical irritation as a cause of carcinoma of the skin cannot be illustrated better than by the "horn-core" of draught cattle in India, which is a carcinoma developing at the root of the right horn, by which the animal is attached to a waggon or agricultural implement

At the present day the occurrence of carcinoma as a sequela of the dermatitis resulting from repeated exposure to X-rays is of especial

interest, and a striking example of a chronic inflammatory lesion passing imperceptibly into malignant disease. Rowntree, who has made a study of this subject, found that, up to 1909, 11 cases of X-ray carcinoma had been recorded. In 5 of these 11 cases the growths, which appear as typical carcinomatous ulcers, were multiple, occurring on different fingers or on both hands, and in one case on both hands and on the chin. In the occurrence of pigmentation *and warty growths, the dermatitis* produced by X-rays closely resembles xerodermia pigmentosum, a disease in which squamous carcinoma also occasionally supervenes. *By exposing the tails of rats* to the prolonged action of X-rays, Rowntree was able to study the changes occurring in the skin He found that in the most exposed parts the changes were of an atrophic nature, both as concerned the epidermis and the epidermal appendages of the corium. In parts less directly exposed, the changes in the epidermis and its appendages were of a hypertrophic nature The contrast between these two results was very striking in the rabbit's ear, the atrophic changes being seen in the exposed surface, and the hypertrophic changes being produced *by penetration of the rays to the opposite surface. It is apparently* by the stimulating effects caused by moderate degrees of exposure for long periods that X-rays produce warty epithelial overgrowths, and in some instances actual carcinoma. It is a fact of the greatest interest and practical importance that the rays can in certain circumstances cause the development of malignant growths similar to those which in other circumstances they retard or even destroy.

Carcinoma of the scalp sometimes arises in a sebaceous cyst, and may begin as a papillary growth into its interior, only at a later *stage extending beyond the cyst-wall and involving the skin.* The tumour may then form a very prominent vascular mass which may be closely imitated by the simple ulceration of a sebaceous cyst with the formation of exuberant granulation tissue from its exposed interior (p. 626).

Carcinoma of the face and neck is not uncommon (Fig. 136), but varies much in its clinical aspects, being in some instances of slow growth and difficult to distinguish from a rodent ulcer. On the face, as elsewhere, the growth may originate in an ulcer or scar, and is occasionally seen *as a sequela of tuberculous lupus,* beginning most commonly in the scar left by the disease, but sometimes arising from a patch which is still ulcerated.

Hutchinson has called attention to a form of carcinoma of the skin of the face to which he has applied the name "*crateriform ulcer.*" The growth usually begins as a painless papule which, after reaching a certain size, breaks down into a large central cavity. The tumour is usually of rapid growth, but apparently *shows little tendency to affect*

the lymphatic glands, or to recur after removal. It has been suggested that it may arise in the sebaceous glands.

In the neck it occasionally happens that a hard, deeply seated tumour, clearly not originating in the skin, proves to present the structure of a squamous carcinoma. In such cases it is most probable that a small primary growth in some part of the mucous membrane of the throat such as the sinus pyriformis has escaped detection, and



Fig. 136.—Ulcerated carcinoma of cheek.

(From a patient under the care of A. E. Barker.)

that the tumour of the neck is a secondary glandular deposit. We have met with two cases of this nature in which it appeared probable that a secondary carcinoma in the lymphatic glands of the neck had resulted from a primary growth on the lip that had healed spontaneously. In one of these cases, that of a man under the care of Christopher Heath, the tumour, which formed a hard mass below the jaw, proved after excision to be a squamous carcinoma, and there was a history of a small ulcer on the lip which had healed after cauterization, leaving a small scar. In the other case, a small sore on the lip

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Rodent carcinoma is a striking instance of a tumour which, although undoubtedly a malignant growth, manifests its malignancy only by its slowly progressive destruction of the surrounding tissues, and in its most typical form presents the features of an ulcer without any definite clinical evidence of the new growth which the microscope reveals in its base and edges. The histological structure of the tumour is best studied in sections of the small, hard papule which usually represents the earliest stage of the disease. If such a section be examined microscopically a very well-marked epithelial new growth is found beneath the epidermal layer of the skin, which, although much thinned, is continuous over the new growth (Fig 137). The growth consists of

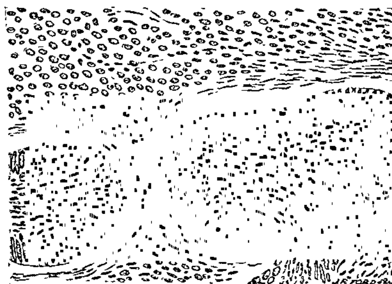


Fig. 138.—Microscopic section of rodent carcinoma, more highly magnified to show the characters of the epithelial cells.

large and often very irregular masses of epithelial cells, those lying next the stroma forming a single layer of columnar cells, while the remaining cells are small and elongated or irregular in shape (Fig. 138). The cells show no tendency to undergo the horny change met with so commonly in squamous-cell carcinomas, and thus cell-nests are not present, and further, the cells are smaller and more irregular in shape, and prickle-cells are not present In the larger cell masses the central cells may undergo a granular degeneration, and small cystic spaces occasionally result. The stroma usually consists of a richly cellular fibrous tissue The structure characteristic of rodent ulcer is found not only in the early papular stage, but also in the base and edges of the later ulcerated stage. The origin of the growth has been the

which healed spontaneously was followed by the growth of a large tumour on the same side of the neck, which soon ulcerated and proved fatal

Mention must also be made of cases in which a deeply seated cystic tumour of the neck presents, in the solid tissue composing its wall, the structure of a carcinoma, usually of the squamous-celled type. Since



Fig. 137.—Microscopic section of rodent (basal-cell) carcinoma.

Volkmann first called attention to such tumours in 1882, numerous cases have been recorded. The tumours are usually situated at the side of the neck, beneath the sterno-mastoid, and intimately connected with the large vessels; the cysts may have a rugose or even papillary inner surface, and present the characters of a tumour developing in a cyst rather than of a cystic change in an originally solid tumour. It thus seems very probable that this form of deeply seated cystic carcinoma arises, as suggested by Volkmann, in remnants of a branchial cleft (branchiogenetic carcinoma).

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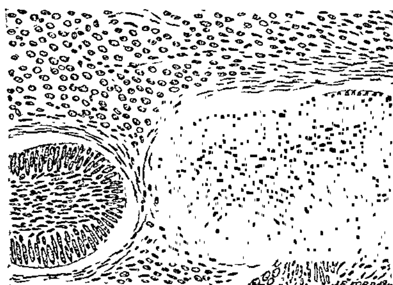


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occasion of much discussion, but, as already stated (p. 555), it is now generally regarded as a basal-cell carcinoma arising in the basal layers of the epidermis or hair-follicles

The small, firm, red pimple as which the disease usually starts, *often after remaining unchanged for long periods or only slightly enlarging*, becomes later covered with a small crust, on removing which the papule is found to be superficially ulcerated, and gradually the papule is replaced by an ulcer which *very slowly extends, chiefly in area.* Such a *rodent ulcer* presents a pinkish granular or furrowed surface, often covered by crusts, and the edges may be almost clean cut, but more often are rolled or slightly beaded. The base and edges are often distinctly indurated, and sooner or later the ulcer becomes adherent to the deeper tissues. As the ulcer slowly and painlessly increases in area, it also usually increases in depth, and when occurring in its favourite positions on the face or anterior part of the scalp, it may open up the nasal cavity invade the orbit, or by destroying the underlying skull expose the dura mater. It is not uncommon to notice some *temporary attempt at healing at part* of the edge of the ulcer, but it is rarely that this proceeds far enough to cause any cicatricial shrinking, and thus, should part of one of the eyelids be destroyed, the remaining portion shows little or no displacement or interference with its movements Rodent ulcer usually occurs on the upper part of the face, especially in the neighbourhood of the inner canthus, or on the frontal and temporal regions of the scalp. In other situations it is very rare

It is a remarkable feature of the disease that it may progressively

rodent carcinoma is rarely met with before middle age, but often in such cases a pimple has been present for many years. It is more common in men than in women. Sequeira has recorded the case of a girl in whom a pimple on the lower eyelid, first noticed in the sixteenth year, developed into a rodent ulcer, and another in which it began at the age of 11. *In the former case the patient lived with an uncle* who had a large rodent ulcer on the forehead.

Rodent ulcer is occasionally multiple, but it is very rarely that the growths exceed three or four in number Adamson has, however, recorded two cases in which the separate lesions, some nodular and others ulcerated, numbered respectively twenty or more and thirteen

The **diagnosis** of rodent ulcer from syphilitic and tuberculous ulcers is rarely difficult, and from an ordinary *squamous-cell carcinoma* the diagnosis is based not only on the absence of definite tumour masses, but also on the prolonged course of the disease and the

absence of glandular invasion. Occasionally, however, the histological structure usually associated with a rodent ulcer is found in a tumour presenting clinical features much more like those of the common fungating form of cutaneous carcinoma, and cases also occur in which the tumour, instead of appearing as a depressed ulcer, takes the form of a slightly raised plaque, not necessarily ulcerated on the surface (Fig 139)

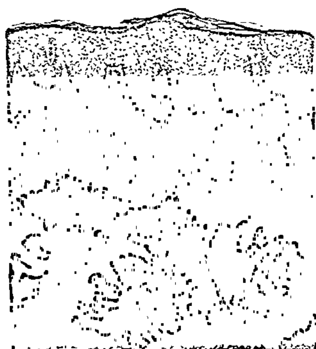


Fig. 139.—Microscopic section of small non-ulcerated tumour of skin, having the histological structure of rodent carcinoma. (The tumour was removed by Lord Lister from the buttock.)

It will thus be seen that the differential diagnosis between the basal-cell carcinoma of the skin and the ordinary squamous-cell form may be impossible without microscopic examination. Darier has indeed shown that tumours having an intermediate structure are occasionally met with.

The results of the treatment of rodent ulcer by irradiation are much more favourable than in any other form of malignant growth. It is indeed the only form of malignant tumour in which irradiation can be selected as an alternative to operation even when the tumour is in an early and operable condition. Radium is preferable to X-rays for the purpose, and can be applied on a suitable skin applicator.

Carcinoma of the lips is common in the lower but rare in the upper lip. Thus, of 211 cases collected by Rowntree, in only 6 was the upper lip the starting-point of the disease. Cancer of the lips is much more common in men than in women, and in a large proportion of cases results from the irritation of the stem of a tobacco

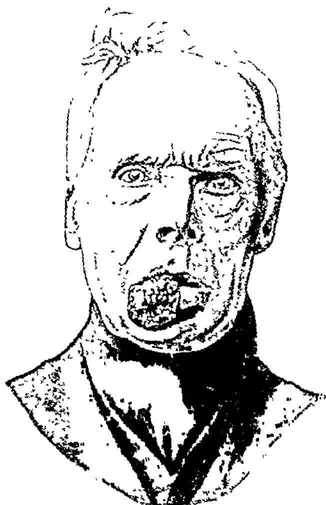


Fig. 140.—Carcinoma of lower lip.

pipe, especially the rough, hot, short stem of the labourer's clay-pipe, and the name "countryman's lip" has been applied to it (Fig. 140). The average age at which the disease begins is 55 years. It usually begins on the edge of the lower lip, about midway between the middle line and the angle of the mouth, as a small, warty growth, fissure, or ulcer. Beneath the surface a definite button-like induration can be felt even in the early stages. As the disease advances, an irregular

ulcer having the characters already described in squamous carcinoma of other parts of the skin results. The lymphatic glands first invaded are those of the submental or submaxillary groups.

Carcinoma beginning in the upper lip, especially if near the middle line, tends to spread to the alveolar border and to the columella, but laterally shows sometimes a tendency to be limited by a line a short distance from the angle of the mouth. The glands chiefly affected are the submaxillary, the maxillary which lie on the surface of the lower jaw at the anterior border of the masseter, and sometimes the buccinator group which lie in the substance of the cheek.

It is doubtful whether the removal of a small carcinoma of the lower lip by the usual V-shaped incision is an altogether satisfactory method, and it is probably better to adopt the method advised by Cheatle, in which the incisions, starting from the margin of the lip, diverge at first and then converge to meet below the lower border of the jaw. In more extensive cases a plastic operation is necessary to repair the lip. In all cases the corresponding glands, whether palpably enlarged or not, should be removed, and if the disease is near the middle line of the lip this should be done on both sides.

Carcinoma of the tongue is unfortunately of very common occurrence, and is discussed at length in another part of this work, so that only certain points bearing on the general features of the disease need consideration here. The growth may arise at any part of the surface of the tongue, but the favourite site is the lateral border at or about its middle. Other important situations are the dorsum, where the growth is particularly liable to be confused with gumma; the extreme base, where the disease may be overlooked until it has reached an advanced stage, and lastly the under surface, often near the frænum, where the growth tends to invade the floor of the mouth and the mandible. The tumour almost always has the structure of a squamous-cell carcinoma, and, as in other situations, may assume a warty or an ulcerating form, whilst in the large majority of cases some definite precancerous condition can be recognized. In many instances the disease arises at a spot where the tongue has been persistently irritated by a carious tooth, and it is extremely important to recognize that a small ulcer on the border of the tongue which proves intractable and refuses to heal after the removal of any irritation caused by the teeth should be regarded with grave suspicion and excised. In other cases the growth originates in the spot at which the stem of a tobacco pipe habitually comes in contact with the tongue and causes a local change in the mucous membrane similar to the changes met with more diffusely in chronic superficial glossitis.

In the most marked cases of the latter affection, syphilis is the causal agent, but in some instances there is no evidence of a syphilitic

taint and the changes in the mucous membrane are associated with oral sepsis, alcoholic excess, and chronic dyspepsia. The most common manifestation of chronic superficial glossitis is the presence of smooth, white or bluish-white patches (leucoplakia) in which the papillæ are more or less completely absent. In association with this condition fissures and superficial ulcers are common, and another not uncommon result of the chronic inflammation is the formation of a slightly raised warty patch in which the papillæ, instead of shrinking, remain permanently hypertrophied The important part played by this affection of the tongue as a precursor of cancer was first pointed out by Hulke in 1864 The malignant growth may originate in any of the manifestations of the superficial inflammation, but especially in a fissure, ulcer, or warty patch (Fig. 141).

It will thus be seen that carcinoma of the tongue rarely manifests itself as a distinct growth on the previously healthy mucous membrane,



Fig. 141.—Carcinoma of tongue, developing in a warty patch caused by chronic superficial glossitis.
(University College Hospital Museum)

but usually appears as a modification of a previously existing chronic inflammatory lesion. Butlin, whose experience of the disease was unrivalled, recorded a series of cases illustrating the earliest stages of cancer of the tongue—conditions previously regarded as precancerous, but which were proved to be actual cancer by careful investigation in the laboratory of the Imperial Cancer Research Fund. Four conditions were specially described by Butlin: 1, a flat, very slightly raised, smooth, red, glazed plaque, feeling like a thin piece of gristle in the surface of the tongue, and closely resembling a primary syphilitic lesion; 2, a white, warty growth, not ulcerated, and scarcely indurated at its base; 3, a slight thickening and hardening of an old leucoplakic area; 4, a nodular plaque, red, and beginning to ulcerate, with drawing-in of the surrounding tissues.

A carcinoma on the side of the tongue tends at an early stage to draw upon the mucous membrane passing from the tongue to the floor of the mouth, and thus the tongue at the affected part is fixed or

"anchored," so that when protruded the tip deviates towards the affected side As the disease spreads, it tends to assume one of two forms: in one it retains a warty character, and in the other ulcerates and fungates, destroying the substance of the tongue extensively, although sometimes showing a pronounced tendency to be limited by the middle line.

The distribution of the lymphatics of the tongue in relation to the spread of carcinoma and the treatment of the disease has been carefully studied by many observers. A valuable contribution to our knowledge of this subject has been made by Jamieson and Dobson, based on the examination of injected specimens. The glands concerned are (1) the submental group, lying in the triangle formed by the anterior bellies of the digastric muscles; (2) the submaxillary group, lying between the submaxillary salivary gland and the lower border of the mandible, and (3) the deep cervical group, lying along the line of the great vessels. The third group may be divided into an upper set, extending from the tip of the mastoid process to the tendon of the omohyoid, and of which the most important projects at the anterior border of the sterno-mastoid below the angle of the mandible (jugulo-digastric), and a lower set, beneath and behind the lower part of the sterno-mastoid, and of which the jugulo-omohyoid gland is the most conspicuous. In front of the circumvallate papillæ two sets of lymphatics—marginal and central—drain the plexus in the mucous membrane. The marginal vessels, which drain the outer third of the dorsum, the margin, and the under surface, pass to the submental, submaxillary, the jugulo-omo-hyoid and the jugulo-digastric and other glands of the upper cervical group. The central vessels, draining the remainder of the upper surface of the tongue, descend between the genio-hyo-glossi muscles, and reach the deep cervical glands, especially the jugulo-digastric and jugulo-omo-hyoid, and the submaxillary glands. The vessels from one side of the middle line of the tongue pass to glands on both sides of the neck. Lastly, the lymphatics from the plexus in the mucous membrane behind the circumvallate papillæ pass to glands of the deep cervical group. The efferent vessels of the submental glands pass to the submaxillary and jugulo-omo-hyoid glands, those of the submaxillary group pass to the jugulo-digastric and jugulo-omo-hyoid glands and those between them Probably the jugulo-digastric gland is most frequently the first that is palpably enlarged, and can be felt slightly below and behind the angle of the mandible.

Lenthal Cheatle, from his observations on the mode of spread of cancer in the substance of the tongue, believes that it is determined largely by the arrangement of the muscles He finds that when the disease begins in the anterior two-thirds of the organ, the hyo-glossus

is the muscle first invaded, and, in a case in which the tongue had been removed by an intrabuccal method, a deposit of growth was found in the part of this muscle which had been left.

Treatment.—It is impossible here to refer to the operative methods employed in the removal of carcinoma of the tongue in the different situations in which it may occur. In a very early case, when the local condition is very likely suspicious rather than evidently malignant, it should be sufficiently freely excised by incisions so arranged that the edges of the wound can be brought together by sutures. The diseased tissue is carefully microscoped, and if it

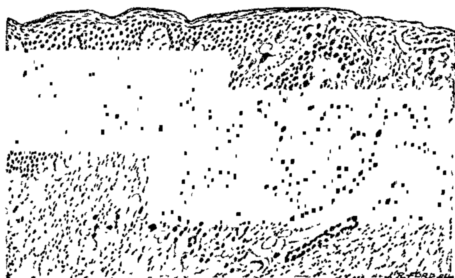


Fig. 142.—Microscopic section through edge of small carcinomatous ulcer of tongue, showing irregular downgrowth of epithelial cells into the tissues beneath the floor of the ulcer.

prove to be carcinomatous (Fig. 142), a subsequent operation for the removal of the lymphatic glands must be performed.

Jamieson and Dobson's investigations show, first, that removal of the submental, submaxillary, and the upper and lower deep cervical glands is necessary in all cases, and secondly, that the operation should be performed on both sides of the neck in growths (*a*) of the tip and frænum, (*b*) of the dorsal surface, (*c*) of the back of the tongue, and (*d*) of the lateral border, which have spread towards the middle line. Only in cases of marginal growth which has not spread forwards or backwards or to the upper surface to any extent is the unilateral operation adequate. The complete gland operation ("block dissection" of Crile) always includes removal of the submaxillary salivary gland, and often of the sterno-mastoid and internal jugular vein.

Carcinoma of the jaws is represented by two distinct forms of tumour: (1) carcinoma of the mucous membrane of the gums or hard palate, and (2) carcinoma of the mucous membrane lining the maxillary antrum.

1. Carcinoma beginning in the mucous membrane of the gums or hard palate is usually of the well-marked squamous-cell variety, and, on account of the close connexion of the mucous membrane with

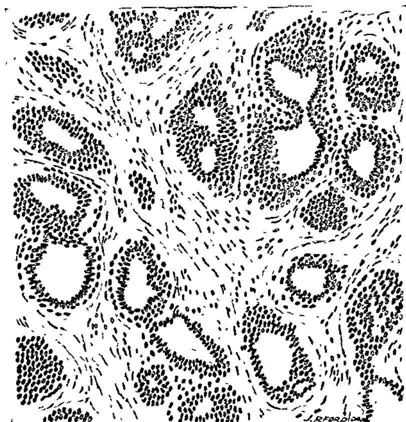


Fig. 143.—Microscopic section of tubular carcinoma of antrum.

the periosteum, tends at an early stage to involve the bone In some cases, especially on the gums, the disease assumes a warty form, and is apt to be mistaken for a simple papilloma. In other cases the growth begins as an ulcer and, as it advances, causes loosening of the teeth, and exposure or even necrosis of part of the alveolus. The condition may thus simulate simple necrosis, the fungating masses of the ulcerating growth being mistaken for the prominent granulations around a sequestrum. Carcinoma does not often begin in the mucous

membrane of the hard palate, but is very serious on account of its liability to invade the antrum and thence to extend in a manner similar to a tumour beginning primarily in that cavity. An ulcerating carcinoma of the hard palate may present very little evidence of new growth, and for this reason is liable to be mistaken for syphilitic ulceration.

2. Carcinoma of the **antrum** presents considerable variations in its histological structure, dependent probably in part upon whether it arises in the columnar epithelium of the surface of the mucous membrane, or in the mucous glands. In some recorded cases the tumour assumes a papillary form, and has the structure of a columnar-celled carcinoma, but more often it occurs as a soft, solid tumour indistinguishable with the naked eye from the sarcomatous tumours which also arise in this situation. Tumours of this form vary in their minute structure, sometimes having that of a spheroidal-cell carcinoma, whilst in others the alveoli present a lumen surrounded by several layers of spheroidal or polyhedral cells (tubular carcinoma, Fig. 143), or by cells having a more or less columnar shape.

A carcinoma of the antrum may fill the cavity without producing much external evidence of the serious nature of the disease. Later it tends to penetrate the bony walls of the cavity, encroaching upon the cheek, orbit, nasal cavity, or mouth, or projecting backwards into the naso-pharynx or pterygo-maxillary region. Extension of the disease in the last-mentioned direction is unfortunately sometimes discovered during operation upon a case regarded as favourable for complete removal.

Carcinoma of the pharynx has been specially studied by Trotter in relation to the symptoms produced by the disease and the nature of the operative procedures required for its removal He has suggested the following classification of growths in this region: (1) naso-pharyngeal, (2) oro-pharyngeal, (3) epilaryngeal, (4) tumours of the pyriform sinus, and (5) hypopharyngeal. In the naso-pharynx squamous-cell carcinoma is very rare, malignant growths in this region being usually endotheliomas or sarcomas. The oro-pharyngeal group includes carcinoma beginning in the tonsil, the anterior pillar of the fauces, and the pharyngeal part of the tongue. When beginning in the tonsil or spreading to it from the faucial pillar, the growth tends especially to spread downwards towards the pyriform sinus. The epilaryngeal group of Trotter includes growths beginning in the epiglottis or aryteno-epiglottic fold, and usually described as extrinsic carcinoma of the larynx. The pyriform sinus is the recess or diverticulum of the pharynx between the ala of the thyroid cartilage and the upper aperture of the larynx, and carcinoma beginning in this region is especially liable to escape detection even when secondary deposits have already formed in the cervical glands. The hypo-

pharyngeal growths affect the lowest part of the pharynx, including the post-cricoid region, and occasion early difficulty in swallowing It is interesting to note, as pointed out by Trotter, that in this last situation carcinoma is most common in young and middle-aged women, whereas in all other situations in the pharynx it occurs chiefly in middle-aged and elderly men.

Carcinoma of the nasal cavity is not common. It may be of the squamous-cell or spheroidal-cell form, and the most common situations in which the disease starts are the septum, the anterior parts of the floor and outer wall, and the ethmoidal region. The growth tends to spread into neighbouring cavities such as the antrum, and in some cases the nature of the disease may be obscured by the presence of nasal polypi.

Carcinoma of the salivary glands is rare, and is always of the spheroidal-cell form. It is less rare in the parotid than in the other glands, and may occur as a growth of considerable hardness, or in a softer form indistinguishable clinically from a sarcoma. The distinction between a malignant growth of the parotid gland and an endothelioma in the parotid region is rarely difficult; the former presents itself as a deeply fixed tumour, filling the hollow behind the ramus of the jaw, whereas the endothelioma is usually, in the early stages at least, more superficially placed and often freely movable. Paralysis of the facial nerve may result, and in the case of a tumour in the parotid region is to be regarded as a certain indication of its malignant nature

In the later stages a carcinoma of the parotid gland may involve the skin and ulcerate, the condition closely resembling that resulting from an ulcerated squamous carcinoma of the skin with secondary deposits in the lymphatic glands of the parotid region.

Carcinoma of the thyroid gland is usually of the spheroidal-cell form. The disease tends to develop in glands which are already the seat of a simple enlargement, and is therefore met with most commonly in localities in which goitre is endemic. Berry has pointed out that, even when a history of pre-existing enlargement cannot be obtained, the presence of cysts or of areas of calcification in the tumour often affords evidence of previous disease of the gland

The histological characters of the tumour vary within wide limits. In some instances, as in the tumour illustrated in Fig. 144, the structure is essentially spheroidal-celled; in other cases the epithelium assumes a more cubical form and surrounds a definite lumen; whilst in certain rare forms of carcinoma the tumour retains, in both the primary and secondary deposits, a striking resemblance to the normal thyroid tissue, and consists of alveoli containing colloid substance. Still more rarely

the tumour has a papillary structure, and in more than one recorded case of this nature the same structure was presented by the secondary deposits in the lymphatic glands.

In its macroscopic features carcinoma of the thyroid presents equally marked variations. In rare cases the whole gland is infiltrated by a soft growth, which, except on microscopic examination, is indistinguishable from a sarcoma. More commonly the tumour is hard and nodular, and, if limited to part of the gland, may present such a degree of encapsulation as to produce a close resemblance to a



Fig. 144.—Microscopic section of carcinoma of thyroid gland.

simple adenoma. Lastly, it is very important to bear in mind that in certain cases of carcinoma of the thyroid the naked-eye appearances of the disease are indistinguishable from those of a simple colloid goitre.

At a comparatively early stage a carcinoma of the thyroid tends to encroach upon the structures outside the capsule, and the tumour thus becomes fixed. Extension to the trachea is most common, the growth involving and finally ulcerating through the mucous membrane. Berry states that although the muscular wall of the pharynx is often implicated, the tumour very rarely penetrates the mucous membrane. By its further growth the tumour may become adherent

to and even surround the large vessels of the neck, and may cause paralysis of the recurrent laryngeal and sympathetic nerves.

Metastases are very common in carcinoma of the thyroid, some forms affecting particularly the lymphatic glands of the neck and thorax, and others occurring by way of the blood-stream The frequency of the latter is no doubt explained by the character of the blood-vessels, which often have not the usual form of capillaries, but are irregular sinusoid spaces in the very delicate stroma, the endothelium bounding them being in direct contact with the epithelial cell-masses

The metastases are particularly common in the bones, which, according to Limbacher, are affected in 37 per cent. of the cases These secondary bone deposits are sometimes remarkable for the extraordinary way in which their structure imitates that of normal thyroid tissue, and also in the fact that they may pulsate. The first cases of this nature were recorded by Cohnheim and Max Runge in 1876, and were followed, in 1880, by Morris's case in this country. In the latter, secondary growths were present in the left parietal bone, right clavicle, and both femurs, and it was only after investigation by a committee of the Pathological Society, consisting of Marcus Beck, Butlin, and Godlee, that the relation of the bone tumours to an enlargement of the thyroid gland was established. Since that date numerous similar cases have been recorded.

The great clinical importance of this aspect of carcinoma of the thyroid depends upon the fact that a secondary bone deposit may alone engage the attention of the surgeon, while the existence of an enlargement of the thyroid may be overlooked or disregarded Many mistakes of this kind are on record, and in more than one instance a pulsating secondary tumour of the sternum has been mistaken for a thoracic aneurysm

Hebb has recorded the case of a man aged 41 who was admitted into the Westminster Hospital suffering from paraplegia and angular curvature of the upper dorsal spine The symptoms were of two years' duration, and were accompanied by great emaciation At the post-mortem examination a mass of growth was found involving the bodies of the second, third, and fourth dorsal vertebræ and causing pressure on the spinal cord. There were also numerous secondary growths in the lungs and kidneys In the isthmus of the thyroid body was an encapsuled, partly cystic tumour as large as a hen's egg. The primary and secondary growths consisted of follicles, lined with [illegible]

ment of the thyroid as unimportant. A careful examination of the

breast, thyroid, or prostate may afford valuable evidence in cases obscure bone tumours, or in cases suspected to be instances of tub culous disease of the spine in middle-aged or elderly subjects.

In considering the histological variations of carcinomas occurri in connexion with the thyroid gland, Langhans refers to tumo probably arising in the parathyroids, as described by Kocher, as well to others possibly originating in the lateral thyroid rudiment to whi attention was first drawn by Getzowa.

Carcinoma of the larynx is almost invariably of t squamous-cell form, but a few instances of columnar-cell growt probably originating in the mucous glands, have been recorded. *a rule, the disease arises independently of any pre-existing pathologic* condition, and, contrary to what might be expected, it is said th there is no evidence that it occurs as a sequela of pachydermia the larynx. The form of carcinoma usually known as extrinsic carc noma of the larynx has already been described as the epilaryngе variety of carcinoma of the pharynx (p. 570). In the larynx prop the disease usually begins in the vocal cords or ventricular bands it mostly pursues a slow course, and invasion of the cervical lymphat *glands is often absent up to a late stage*

The growth presents the same variations in its naked-eye appea ances as are seen in squamous-celled carcinoma elsewhere, and ma be warty or ulcerating. On the vocal cords the earliest sign of th disease may be, according to Semon, a unilateral congestion, a diffus red uneven infiltration, a broad-based wart, or an uneven fringe-like out growth. Impaired mobility of the affected cord is an important sign

Carcinoma of the lung may be of the spheroidal-cell o cubical-cell form. It may commence in the hilum of the lung, origin ating probably in one of the bronchi, or in the centre of the lung having its origin either in the alveolar epithelium or in the epitheliun *of the bronchioles. In both forms secondary deposits in the bronchia* glands are common. When the growth originates in the hilum i tends to spread into the lung tissue and to obstruct the bronchi leading to pulmonary collapse and bronchiectasis, and it may caus diffuse infiltration of the pleura. A carcinoma beginning in the substance of the lung may undergo necrosis and give rise to pulmonary hæmorrhage.

Carcinoma of the œsophagus usually occurs as the squamous-cell form, with well-marked cell-nest formations, but in rare instances, possibly when the growth originates in the œsophageal glands, the structure is of spheroidal-cell form, and in tumours at the cardiac orifice the structure may suggest that the growth originated in the stomach. The disease, which is common, especially in men, occurs most frequently at one or other extremity of the

œsophagus, or at the level of the bifurcation of the trachea, where the œsophagus is crossed by the left bronchus. The naked-eye characters of the disease vary widely, and whilst in some cases an annular stricture, fibrous in appearance, results, in other cases the growth involves a considerable length of the canal and leads to very extensive ulceration. In the ulcerating forms the growth frequently spreads through the wall of the œsophagus leading to a fistulous communication with the trachea or bronchus opening up a neighbouring blood-vessel, or causing suppuration in the adjacent tissues of the neck or thorax. The extent of the glandular invasion varies greatly, being sometimes absent, sometimes limited to the cervical glands, and in other cases producing a large mediastinal tumour.

Carcinoma of the stomach.—The stomach is one of the three organs in which carcinoma most commonly occurs, the other two being the breast and the uterus.

In its minute structure carcinoma of the stomach presents two forms, the epithelial cells in one having an undifferentiated spheroidal-cell form, and in the other retaining a more or less cubical or columnar shape (Fig 145). No sharp line can be drawn between these two varieties, but while the former tends to manifest itself as an ulcer or induration or as a fungating tumour, the columnar-cell carcinoma almost always assumes the fungating form Occasionally the growth undergoes extensive colloid degeneration. The evidence, both clinical and pathological, that carcinoma may originate in a chronic gastric ulcer is very convincing. The clinical evidence is afforded by the fact that in a considerable proportion of cases there is a long antecedent history of symptoms suggestive of chronic gastric ulcer The pathological evidence has been studied chiefly at the Mayo Clinic in America and by Moynihan and Sherren in this country. Moynihan finds that in 25 to 30 per cent. of carcinomas of the stomach removed by operation the malignant change appears to have originated in a chronic ulcer, and that in 10 per cent. of apparently simple ulcers removed by operation microscopic examination shows the appearances of early carcinoma. Sherren found similar evidence in 22 out of 69 carcinomas of the stomach removed by operation, and in 11 out of 165 apparently simple ulcers carcinoma was found in the edge of the ulcer.

The favourite site of carcinoma of the stomach is the small curvature near but not at the pylorus. Less common situations are the posterior surface and pylorus, whilst more rarely it occurs at the great curvature or cardiac orifice.

As seen at an operation, unless the growth has spread to the peritoneal surface producing opaque patches, or caused metastases in the glands or elsewhere, a malignant ulcer cannot certainly be distinguished from a simple chronic one, and the amount of induration is no guide.

As already mentioned, microscopic examination may afford the only proof that a chronic ulcer is malignant. Sometimes, however, it is possible to recognize with the naked eye the malignant change in a chronic ulcer, one part of it presenting a hard, craggy, raised edge.

A carcinoma beginning in the region of the pylorus tends to spread into the body of the stomach but not into the duodenum. It extends chiefly in the submucous tissue, often especially along the curvatures, and tends to invade the lymphatic glands which lie in the small omentum

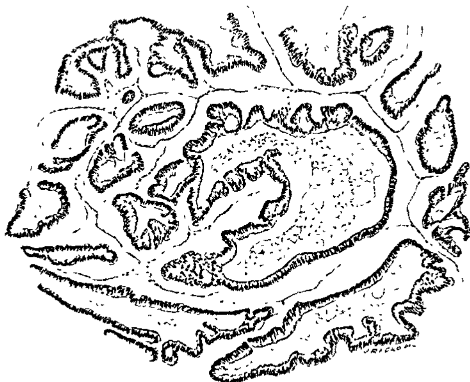


Fig. 145.—Microscopic section of columnar-cell carcinoma of stomach.

and along the right half of the great curvature between the layers of the great omentum. A consideration of the mode of spread of carcinoma of the pylorus shows that in the removal of the disease by operation the duodenum may safely be divided a short distance from the growth, but that in the stomach the section must be made in such a way as to include the whole length of the small curvature and a corresponding part of the great curvature, whilst, in dividing the omenta attached to the portion of stomach removed, the section must be so planned as to remove the glands along the two curvatures.

Among other forms assumed by carcinoma of the stomach is that

in which the disease, usually beginning in the region of the pylorus, gradually involves a large part of the organ by extension along the submucous coat, producing a condition of general contraction and thickening which presents itself as one form of "leather-bottle stomach." In the fungating form of the disease an irregularly globular or cauliflower-like mass of growth may project into the cavity of the stomach, or the tumour may involve a considerable area in the form of a less prominent, irregularly excavated mass.

An ulcerated carcinoma is less likely than a simple ulcer to lead to perforation, and erosion of a large vessel is relatively rare. When the fungating tumour is of the more highly specialized columnar-celled type the tendency to invasion of the lymph-glands is much less than in the case of tumours of the undifferentiated structure. In advanced cases of carcinoma of the stomach various extensions of the disease may occur. Thus, secondary deposits in the liver may occur by way of the portal circulation or from the portal lymphatic glands; the left supraclavicular glands may be invaded; extensive peritoneal infection may occur by lymphatic permeation, causing diffuse thickening; while sometimes the pelvic viscera, especially one or both ovaries, may be involved. This occurrence of secondary deposits in the pelvis may lead to mistakes in diagnosis, as, for instance, if the ovaries are involved while the tumour of the stomach is still unproductive of marked symptoms, and as in a case under the care of Bilton Pollard in which infiltration of the peritoneum of the recto-vesical pouch led to the diagnosis of primary carcinoma of the prostate. It will thus be seen that in any case in which carcinoma of the stomach is suspected, examination of the rectum and of the left supraclavicular region should never be omitted.

Carcinoma of the liver.—Primary cancer of the liver is rare, whereas secondary deposits, especially when the primary growth is situated in the area drained by the portal vein, are very common.

Primary carcinoma may originate in the liver cells, or in the intra hepatic biliary passages. In the first variety the tumour has the structure of spheroidal-cell carcinoma, whilst in the other it usually retains more or less distinctly the columnar shape of the cells. To the naked eye the three most important forms of primary cancer of the liver are—(1) a soft, solid mass in the substance of the organ, usually the right lobe; (2) a diffuse form associated with cirrhosis; and (3) multiple nodules associated with cirrhosis. The liver may also be invaded by the direct extension of a carcinoma originating in the gall-bladder or extrahepatic ducts.

Carcinoma of the gall-bladder is much more common in women than in men, and is associated with the presence of gall-stones in probably 80 or 90 per cent. of the cases. Such a relationship cannot

be accidental, and there can be no doubt that the changes in the mucous membrane resulting from the long-continued irritation of calculi is a factor in the causation of the malignant disease. The tumour may be of the columnar-cell variety, or may have an undifferentiated form, whilst in a few recorded cases a squamous-cell growth has resulted from a metaplasia similar to that sometimes occurring in other mucous membranes normally lined with columnar epithelium. The growth usually tends to infiltrate the wall of the gall-bladder, forming eventually a solid mass of growth with gall-stones embedded in its centre. Colloid degeneration may occur, and in rare cases the tumour assumes a polypoid or papillary form. As the disease extends, it is very liable to infiltrate the adjacent parts of the liver, or other neighbouring parts such as the colon or pylorus may be involved. Secondary deposits are likely to be found in the glands in the portal fissure, but metastases elsewhere are very rare.

In the **large biliary ducts** carcinoma is most frequent at the junction of the cystic and hepatic ducts and at the termination of the common bile-duct, and is an important cause of obstructive jaundice. The character of the growth is similar to that occurring in the gall-bladder, and it may present itself as a nodular mass in the lumen, as a dense growth surrounding the duct, or as a warty or villous excrescence. Carcinoma of the termination of the common bile-duct begins in the ampulla of Vater and may present itself as a small flat ulcer in the duodenum or as a fungating or papillary projection Unlike carcinoma of the gall-bladder, the disease occurring primarily in the ducts is rarely associated with gall-stones

Carcinoma of the pancreas is rare. Among 2,005 cases of carcinoma examined post-mortem, collected by Biach from three Vienna hospitals and quoted by Robson and Moynihan, the pancreas was the seat of the disease in 29 cases. The tumour is usually a spheroidal-cell growth of the hard variety, but the growth may be columnar-celled, and sometimes presents colloid degeneration. In very rare instances cystic changes in the tumour have been so pronounced as to constitute one variety of pancreatic cyst. A hard carcinoma in the head of the pancreas, which is by far the most common form of the disease, is of great clinical importance as a cause of obstructive jaundice often associated with considerable distension of the gall-bladder.

Carcinoma of the intestine is usually columnar-celled (Fig. 131), but the degree to which the columnar shape of the cells is preserved varies very greatly, so that, as already described, whilst in some tumours the alveoli are in parts lined with a single layer of columnar cells, in others the cells proliferate irregularly and partly fill the lumen, and in yet others the columnar type is so entirely lost

that the growth has a spheroidal-cell structure. Carcinomas of the intestine not uncommonly undergo extensive colloid degeneration. The change begins with the appearance in the cell protoplasm of clear, colourless, highly refracting droplets, which gradually enlarge and coalesce until the cell is replaced by a gelatinous mass. By the fusion of the adjacent cells the alveoli become filled by a jelly-like substance, so that in those parts of the tumour in which the change is most emphatic all evidence of its epithelial nature may be lost. To the naked eye a colloid cancer presents the appearance of a delicate fibrous meshwork, the spaces of which are filled with the colourless or yellowish-brown translucent material.



Fig. 146.—Carcinoma of jejunum.

In all parts of the intestine a carcinoma may be met with in three chief forms of growth—as a shrinking fibrous form causing an annular stricture, as an ulcer presenting the characters already described (p. 548), or as a fungating or papillary mass projecting into the lumen of the bowel. In passing along the intestine from the pylorus to the anus very striking differences are observed in the liability of the different parts to the development of carcinoma. Throughout the small intestine it is rare, and in the large intestine common. In the large intestine, although any part may be affected, it is most common at the ileo-colic valve and cæcum, at the hepatic and splenic flexures, and above all in the sigmoid colon and rectum.

Carcinoma of the small intestine is rare. In the duodenum it is almost unknown, except when occurring in the ampulla of Vater. In the jejunum (Fig. 146) and ileum, carcinoma is of very rare occurrence, but is more common in the proximal and distal

portions than elsewhere. It may present any of the features above described, and in its minute structure may be of the columnar-cell or the spheroidal- or polyhedral-cell form (Fig. 147). The effects of the disease and the complications are similar to those met with in the large intestine, and on account of the fluid nature of the contents there may be a striking absence of symptoms *until almost complete* obstruction occurs. Intussusception may be caused by the growth,



Fig. 147.—Microscopic section of the carcinoma illustrated in Fig. 146.

as in the tumour illustrated in Fig. 146, which was situated in the upper part of the jejunum and was successfully removed.

Carcinoma of the large intestine occurs chiefly in the situations *already indicated, and when causing an annular* " malignant stricture " is one of the most common causes of chronic intestinal obstruction. The other conditions which may supervene during the progress of the disease can only be briefly mentioned. As is the case with simple tumours, carcinoma is very liable to cause some degree of *intussusception, very striking instances of which have been met with in* tumours of the ileo-cæcal valve. Secondary deposits are common in the lymphatic glands, liver, and peritoneum, but metastases in the lungs

and bones are very exceptional. The invasion of the peritoneum by lymphatic permeation may reach the extreme degree already described in cancer of the stomach, and if the secondary deposits undergo colloid degeneration, the peritoneal cavity may be extensively occupied by large gelatinous masses. In this connexion it is interesting to recall what has already been said with regard to the condition known as "pseudo-myxoma peritonei," which sometimes follows the escape of mucinous material into the peritoneal cavity from a ruptured ovarian cyst, for the appearances presented to the naked eye, and even under the microscope, may in such cases be very suggestive of colloid carcinoma (p. 473). Striking instances of a similar condition following rupture of the vermiform appendix and discharge of mucus therefrom have been recorded by Fraenkel, Trotter and others. In Trotter's case it was found when the abdomen was opened, about a month after an attack of appendicitis, that the omentum, peritoneum, cæcum, and ascending colon were thickly covered with rounded gelatinous translucent masses, and the case was regarded as one of colloid carcinoma, even after microscopic examination of part of the omentum which was removed. A further study of the specimen and of recorded cases of pseudomyxoma arising from the appendix convinced Trotter that the case was of this nature—a view which was supported by the fact that eighteen months after the operation the patient presented no evidence of abdominal disease.

By the direct extension of the primary growth, fistulous communications with neighbouring parts, such as the bladder, vagina, neighbouring coils of intestine, or even the stomach, may be established, or perforation into the peritoneal cavity may occur. It is, however, a matter of practical importance that when a malignant stricture of the lower part of the large intestine proves fatal by perforation, the perforation often occurs, not at the seat of the tumour, but through the base of one of the multiple follicular ulcers frequently present above the seat of obstruction, especially in the cæcum. An intestinal carcinoma has sometimes been known to extend through the umbilicus, which it has reached by way of the round ligament.

Mention must again be made of the frequency with which an ulcerating carcinoma of the intestine is complicated by suppuration. The practical interest of this lies largely in the fact that the true nature of the disease may be overlooked should abscess-formation occur early in the course of an intestinal cancer which has not yet produced any marked symptoms, as, for instance, when the disease is in the cæcum. It should also be noted that certain inflammatory affections may simulate carcinoma of the bowel. Among such affections the most important is diverticulitis, especially when occurring in the sigmoid colon. The presence of multiple, usually small diverticula

of the mucous membrane which characterizes this condition may lead to various secondary pathological changes, but when a considerable localized fibrous hyperplasia occurs with the production of a tumour-like mass, and perhaps stenosis of the bowel and ulceration, the resemblance to a carcinoma may be very close. Indeed, the distinction has in some instances only been made after resection of the diseased part of the gut, and there can be little doubt that some of the recorded cases in which life has been prolonged for many years after the per-

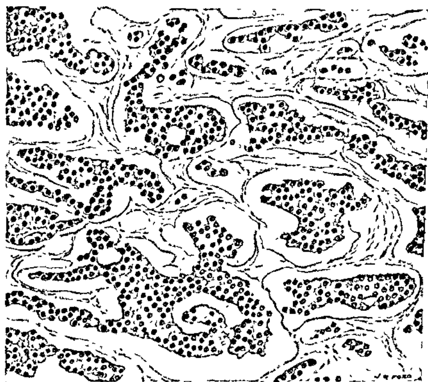


Fig. 148.—Microscopic section of carcinoid tumour of vermiform appendix.

formance of colostomy for a supposed inoperable carcinoma of the colon have been cases of diverticulitis.

In the cæcum also various chronic inflammatory conditions may closely simulate malignant disease, and as examples may be mentioned chronic appendicitis, the hyperplastic form of tuberculosis, and actinomycosis.

Carcinoma of the vermiform appendix is undoubtedly extremely rare. Small nodules, often of a yellowish colour, are not very uncommon in the mucous membrane of the appendix, and have usually been described in cases in which operation has been performed

for appendicitis, sometimes in young subjects. Similar nodules have been met with in other parts of the intestine, and their histological structure closely resembles that of a small spheroidal- or polyhedral-cell carcinoma (Fig 148). Krompecher, who has studied these nodules, believes them to arise in the basal cells between the columnar epithelium cells, and includes them with certain similar tumours occurring in the skin under the name of basal-cell tumours or "carcinoids." They are clearly not malignant.

In speaking of the pathological features of carcinoma of the **rectum** little need be added to what has been said of the disease as it occurs in other parts of the large intestine. The disease is probably twice as common in men as in women, and the average age at which it first produces symptoms is about 50 years It may occur in any part of the rectum, but is particularly common at a distance of two or three inches from the anus. The growth occurs most frequently as a hard, irregular, ulcerated patch (Fig. 149), but not rarely forms a dense, annular, ulcerated stricture, tending to cause a varying degree of invagination. As it extends, the tumour invades the whole thickness of the gut, becoming adherent to and finally invading the surrounding structures, such as the base of the bladder, the prostate, or the vagina. The lymphatic glands first involved are usually those lying between the layers of the mesorectum, whence the iliac and lumbar glands may be invaded. As in other parts of the intestine, the disease is liable to occasion suppuration around the bowel and to cause fistulous communications with the neighbouring viscera.

It cannot be too strongly insisted upon that carcinoma of the rectum may advance even to an inoperable condition without producing any characteristic symptoms, and that its recognition depends solely upon a properly conducted rectal examination.

Carcinoma of the anus is not common, and occurs as the squamous-cell variety, usually beginning at the line of junction of the skin and mucous membrane. Frequently some inflammatory condition precedes the development of the disease; thus, it has been known to begin in an external pile, at the orifice of a fistula, or in the thickened eczematous skin associated with long-standing pruritus ani. The tumour often assumes a very warty form, and thus may be mistaken for the simple papillomatous growths sometimes occurring in the anal region. Secondary deposits are likely to occur in the superficial inguinal glands, and in all cases subjected to operation the glands should be removed from both groins.

Carcinoma of the kidney and ureter.—Under this heading it will be necessary to describe tumours beginning in the renal substance and others arising in the epithelial lining of the calyces, pelvis, and ureter. Of the tumours involving the renal substance,

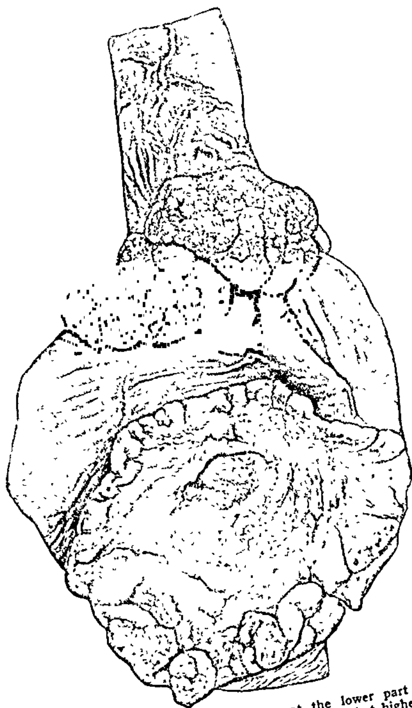


Fig. 149.—Large ulcerated carcinoma at the lower part of the rectum, with a simple villous tumour at a somewhat higher level.

(*University College Hospital Museum.*)

two forms are met with, the diffuse and the localized. In the diffuse form the organ, while still retaining its normal shape, may be greatly enlarged by a soft solid growth. The structure is often tubular and the epithelium cubical. A much more common form occurs as a

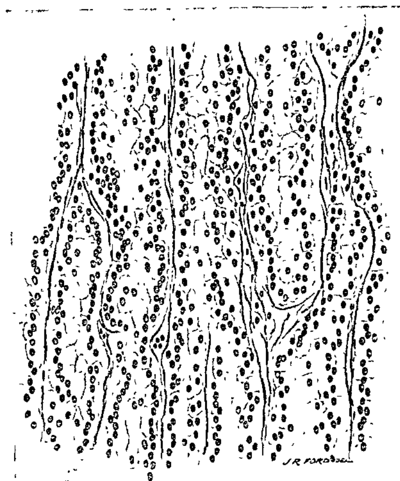


Fig. 150.—Microscopic section of hypernephroma, showing solid columns of polyhedral cells separated by a scanty stroma containing thin-walled capillaries.

localized tumour which displaces rather than invades the renal substance. To this form the name hypernephroma is very commonly applied, although opinions differ as to its origin and real nature. The macroscopic appearances of such a tumour are illustrated in Plate 33. The growth is extremely lobulated, and while some of the lobules present a characteristic orange-yellow colour, others are

dark and hæmorrhagic. The tumour is surrounded by a fibrous capsule, extending in between the lobules, which may be continuous with a more extensive central fibrous mass, resulting from degeneration of the tumour substance and sometimes the seat of calcification. Softening and cyst-formation are sometimes present.

Examined microscopically (Fig. 150), a tumour of this nature is found to consist of solid columns of polyhedral cells. The cells are large, with abundant protoplasm and small *nuclei*; the protoplasm generally contains a great deal of fat, but in some places may present a granular appearance. A tubular appearance may result from degeneration of the central cells of the columns. The latter are separated by a scanty stroma containing thin-walled capillaries. It is stated by some observers that the thorough examination of these tumours will always reveal the presence of a papillary arrangement of the cells in some parts.

In addition to tumours having the very characteristic naked-eye and microscopic characters above described, others are met with which differ from them in greater or less degree. Thus, to the naked eye the extreme lobulation and encapsulation may be less pronounced, and the striking yellow colour absent. Histologically, the tumour may also present different appearances, and in some instances has throughout a definite papillary structure (Fig. 151). The origin of these tumours has been the subject of much discussion and difference of opinion, the question at issue being whether they arise, as the name hypernephroma suggests, in adrenal tissue, or whether they are really carcinomas originating in the renal cells, or lastly whether there are two varieties of tumour.

In connexion with the view that hypernephroma of the kidney is of adrenal origin it may be pointed out that the structure above described has a striking resemblance to that of the zona fasciculata of the adrenal body and of some tumours met with in that organ. Certain other facts may also be noted. It is well known that occasionally the whole or a large part of the adrenal body may be absent from its normal situation and be contained within the renal capsule Numerous observations have shown that, even when the adrenal bodies themselves are normal, rests of adrenal tissue may be found in such situations as the kidney, liver, solar plexus, mesentery, or along the course of the spermatic and ovarian vessels, as, for instance, in the spermatic cord, testicle, and between the layers of the broad ligament. In several of these situations tumours having apparently an adrenal structure have been found. Grawitz, in 1883, first proved that certain small white or yellowish-white nodules occasionally found beneath the renal cortex, and indistinguishable with the naked eye from small fatty or adenomatous growths, are in reality



Hypernephroma.

(From a specimen in the Museum of University College Hospital.)

PLATE 33

'adrenal rests," and suggested that certain renal tumours arise from them.

The clinical course of a renal hypernephroma supports the view that for even long periods the tumour may be benign in nature. Thus, in the case from which the tumour illustrated in Plate 33 was removed, there had been attacks of hæmaturia, associated with discomfort in the left renal region, for a period of seven years; and among the cases collected by Owen Richards, and published in *Guy's Hospital Reports*, are one in which pain had been present for twenty years, and two in which a tumour had existed for thirty-five and seventeen years



Fig. 151.—Microscopic section of carcinoma of the kidney, showing papillary structure.

respectively. Hæmaturia is a very common, and often the first, symptom.

Among 19 cases of renal tumours regarded as hypernephromas, collected by the same writer, in which a post-mortem examination was made, in 4 there were no metastases; in 11 there were metastases by the blood-stream only, chiefly in the lungs, bones, and skin; in 3 there were also glandular deposits, and in 1 peritoneal invasion.

The metastatic deposits in the bones may pulsate, and reference has been made (p. 551) to recorded cases in which an isolated metastasis in one of the bones was present at a time when the primary tumour was still unrecognizable.

All forms of carcinoma of the kidney show a great tendency to extend into the lumen of the renal vein, and may thus reach and distend the vena cava, extending in some instances continuously upwards into the heart. Although a cancer of the kidney may reach a considerable *size while still retained within the renal capsule, the* growth tends sooner or later to extend to the surrounding structures, and thus, for instance, the colon may be involved.

Carcinoma of the **renal pelvis** and **calyces**, and very rarely of the **ureter**, may present itself as a thickening of the wall or as a *papillary growth projecting into the lumen.* In either form the structure is usually that of a squamous-cell carcinoma, although the tendency to form cell-nests is not pronounced. As a result of the obstruction caused by the tumour, hydronephrosis, sometimes with hæmorrhage into it, may occur. It is in this class of renal tumour *that association with calculi has sometimes been noted.* In connexion with papillomas of the urinary tract, reference has already been made to the great difficulty which may present itself in distinguishing a simple papilloma from a villous or papillary carcinoma (p. 483).

Carcinoma of the adrenal.—Tumours having usually a *definitely malignant course are met with in the adrenal, arising some*times in the cortex and sometimes in the medulla. The tumours arising in the cortex have a structure more or less closely resembling that of an adenoma (p. 472) and, as already mentioned, may, when occurring in early life, be associated with precocious sexual development. Bulloch *and* Sequeira, *who have analysed* 11 *recorded* cases of this nature, show that the condition has most commonly been observed in female children, and before the age of 7 years. The most striking feature has been the early growth of hair in the genital regions, and, in boys, on the face, and the premature development of the genital organs. A peculiar dusky tint of the skin has several times been noted. In Adams's case, a boy, puberty set in at 10 years, and was followed by rapid muscular development, and a growth of hair on the face which required to be shaved almost daily. The tumour of the left adrenal was a malignant hypernephroma, and gave rise to metastases in the liver and spleen.

Other tumours, apparently originating in the medulla of the adrenal, present a different structure. In some cases they have been described as round-cell sarcomas, but various *nerve-elements have* been demonstrated in them, suggesting that this view is incorrect and that the tumours really originate from the nervous constituents of the gland. Hutchison has recorded a series of cases of this nature, occurring in children, in which the prominent clinical features were produced *by metastases in the skull,* causing prominent tumours associated with proptosis.

Carcinoma of the urinary bladder. — Carcinoma is by far the most common form of malignant tumour occurring in the bladder. It usually retains, to a varying extent, the stratified character of the normal epithelium (Fig. 152), and in some tumours cell-nests are large and numerous. Little is known of any precancerous conditions in the bladder, but it is interesting that the disease has been observed in aniline workers, and also that in regions in which

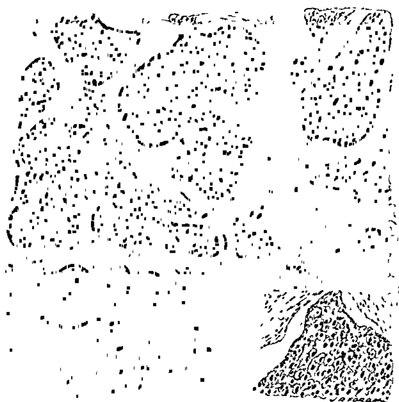


Fig. 152.—Microscopic section of carcinoma of urinary bladder.

bilharzial disease is endemic carcinoma of the bladder may occur in conjunction with it. The association of carcinoma of the bladder with *calculus* is very rare.

The tumour is met with sometimes as a characteristic carcinomatous ulcer, sometimes as a fungating mass projecting into the cavity of the bladder, and sometimes as a papillary growth on an indurated base In the papillary form the villous character is rarely so emphatic as in a simple papilloma, but the essential difference consists in the extension of the new growth into the substance of the bladder-wall.

The tumour most frequently arises from the base of the bladder, usually near the orifices of the ureters. Secondary deposits are common in the pelvic and lumbar lymphatic glands, but are rare in the viscera. In a case recorded by Godlee very perfect cell-nests were found in secondary nodules in the lung, which presented to the naked eye the appearances of a pneumonic area.

Carcinoma of the bladder usually proves fatal by causing a secondary *renal infection.*

Carcinoma of the prostate.—Although the prostate may be invaded by a squamous-cell carcinoma originating in the bladder or urethra, or by a columnar-cell carcinoma of the rectum, spheroidal-cell carcinoma is the only form which occurs primarily in the gland. The tumour is usually of the hard variety, and the extreme hardness and irregularity of the gland are the chief physical signs of the disease. According to Thomson Walker, the average age at which symptoms first appear is 65 years, and as this is practically the same as that of the simple enlargement, the nature of the disease is likely to be overlooked until it is very advanced. The softer forms of carcinoma are rare, and occasionally the growth undergoes colloid degeneration. Evidence goes to show that carcinoma of the prostate not infrequently arises in a gland which is already the seat of the ordinary simple enlargement.

Thomson Walker finds that the growth tends to spread in two chief directions—upwards along the base of the bladder, and laterally towards the sides of the pelvis, obliterating the sulcus which is normally felt with the finger on either side of the gland. The deeply seated position of the growth and the usual absence of ulceration serve to explain the frequent absence of hæmaturia, as compared with a carcinoma of the mucous membrane of the bladder. The most frequent seat of secondary deposits is the intrapelvic lymphatic glands, which may be felt by rectal examination. Walker states that a gland lying just beyond the prostate, close to the vesicula seminalis, is frequently enlarged, and also that in 16 per cent. of cases the inguinal glands are enlarged and hard. In a doubtful case an inguinal gland which was removed was found to contain a secondary deposit of growth.

Carcinoma of the prostate is of special interest on account of the frequency with which secondary deposits occur in the bones. According to Kauffmann, osseous deposits were noted in 14 per cent. of recorded cases, but among 22 cases specially examined for such deposits they were present in no less than 16. Von Recklinghausen found that the bones were affected in the following order, viz. vertebræ, femur, pelvis, ribs, sternum, humerus, flat bones of skull, fibula, tibia, radius, ulna. The secondary deposits exhibit a great tendency

to cause osteoplastic changes in the bones, a peculiarity which is probably connected with the slow growth of the primary and secondary tumours. Thus, in a case recorded by Teale, swellings over the ribs had been noticed for at least two years before death. The secondary tumours originating in the medulla may cause pronounced sclerosis of the bone, and in those situations in which the growth becomes sub periosteal by spreading through the vascular channels in the bone new osseous tissue may also form on the surface.

Blumer, of the Johns Hopkins University, has drawn special attention to the clinical interest of the secondary bone deposits of prostatic carcinoma. The primary tumour, as in Teale's case above-mentioned, may cause no symptoms, and the patient seeks advice on account of the secondary growths. An isolated bone tumour may thus be the only recognized lesion, and is liable to be mistaken for a primary sarcoma. Secondary deposits in the spine may occasion spastic paraplegia, or diffuse deposits without obvious deformity may be manifested by bone pains and spontaneous fractures.

Carcinoma of the urethra, especially in the male, is very [illegible] of the squamous-cell variety. Normally the anterior part of the urethra is lined with a stratified epithelium like that of the glans; whilst in the bulbous portion the lining consists of columnar or sub-columnar cells succeeded by several layers of polymorphous or polyhedral cells, and a gradual transition occurs between this arrangement and that present at the meatus. It is therefore strange, as Shattock points out, that in carcinoma of the bulb a metaplasia should so constantly occur and the resulting growth be squamous-celled. The change may possibly result from the long-standing gonorrhœal stricture which usually precedes the development of the growth. The disease generally simulates a periurethral inflammatory induration in the perineum, and, as in Marcus Beck's case, recorded in 1893, its true nature may only be revealed by a perineal incision. Urethral fistulæ are likely to result. Secondary growths in the inguinal glands appear to be rare, but in one recorded case there were nodules in the lungs.

Carcinoma of the female urethra is usually of the squamous-cell variety, but in two specimens in the Museum of the Royal College of Surgeons the growth is a papilliferous columnar-cell carcinoma.

Carcinoma of the testicle generally occurs as a soft spheroidal- or polyhedral-cell growth, often indistinguishable except by careful microscopic examination from a round-cell sarcoma, and we have already seen that cancer is probably the more common (p. 538). The tumours which have been described as columnar-cell carcinomas

of the testicle must probably be regarded as teratomas (p. 618). A soft carcinoma of the testicle causes at first a smooth enlargement of the organ, but later it becomes nodular as the growth extends through the tunica albuginea. Hæmorrhagic extravasations and necrotic changes are common. Nicholson, from a study of the Guy's Hospital cases, finds that the average age is 43 years. In its extreme malignancy and in the frequency of secondary deposits in the abdominal lymphatic glands the disease behaves in the same way as sarcoma of this organ (p. 538).

Carcinoma of the penis begins most commonly on the surface of the glans, usually in the region of the corona, or on the inner surface of the prepuce, and in structure resembles cancer arising in other parts of the cutaneous surface. It very rarely begins on the body of the penis, and is of extreme rarity in the penile urethra. The relation of the disease to phimosis is well established, and is explained by the changes which supervene in this condition as the result of want of cleanliness and the retention of secretions beneath the tight prepuce. The changes in question so closely resemble those that occur in the surface of the tongue in the condition commonly known as leucoplakia that they need not be described in detail. Thickened whitish areas on the glans, warty patches, and a leathery thickening of the prepuce with fissuring of the orifice are the most important.

The disease, as in other situations, is met with in two forms, the warty and the ulcerating. The importance of recognizing these is great, for while the former may be mistaken for the simple papillomatous growths which are common on the penis, the latter may in its early stages closely resemble the primary syphilitic sore. As the disease extends, the extremity of the penis may become converted into an irregular warty mass, or may be extensively destroyed by the ulceration of the growth. When, as is often the case, the growth is hidden within the tight prepuce, the hardness of the part and the presence of a purulent discharge from the preputial orifice will generally indicate the true nature of the disease. In such a case the prepuce, usually on its dorsal surface, may sometimes become perforated by ulceration, and the diseased glans, protruding through the opening, may cause a very misleading appearance.

The chief paths by which carcinoma of the penis involves the lymphatic glands have been studied by Poirier, Küttner, and others. The glands most likely to be involved are the superficial inguinal group, especially the supero-internal set. It is, however, possible for the disease to reach the glands within the pelvis directly by way of the lymphatics passing through the inguinal and crural canals. Küttner has recorded two cases of cancer of the penis occurring in Bruns's clinic which illustrate an intrapelvic extension of the disease. In

one of these, after amputation of the penis and removal of the glands of the left inguinal region, there was recurrence in front of the bladder. In the second case, two years after amputation of the penis the patient returned with œdema of the right leg caused by a mass of enlarged glands in the pelvis; the inguinal glands were not involved until six months later.

Except in very early cases of carcinoma of the prepuce, which may be treated by circumcision, the penis should be amputated well behind the disease. On account of the connexion between the lymphatics of the two sides of the organ, the superficial inguinal glands should in all cases be removed from both groins.

Carcinoma of the scrotum, or "chimney-sweep's cancer," is probably the most striking instance of the relation between malignant disease and chronic irritation. As the result of the prolonged irritation of soot the skin of the scrotum becomes harsh, dry and thickened, and the seat of small warty excrescences. It is in the latter that the malignant growth usually starts, the wart becoming gradually larger and finally ulcerated. It is an interesting fact that coal miners are not subject to the disease, possibly because coal dust is less irritating than the more finely powdered soot, which readily enters the pores of the skin. The irritation is evidently in some way peculiarly favourable to the development of cancer, for the disease has been seen on the hands of gardeners who used soot for application to the soil, and on the ears of workmen who carried sacks of soot on their shoulders. It has been suggested that the arsenic present in soot is the exciting cause of the dermatitis, which is strikingly similar to that caused by this drug, and it is interesting that in one of the cases of arsenic cancer recorded by Hutchinson the disease occurred on the scrotum. Butlin found that the only satisfactory explanation of the comparative immunity of Continental chimney-sweeps from the disease is that by the use of a protective costume they avoid the constant contact of the part with soot.

In connexion with this subject, it is necessary to refer to Crocker's case, in which a form of dermatitis occurred on the scrotum and penis evidently identical in nature with Paget's disease of the nipple and areola, which is known to be closely associated with carcinoma of the breast (p. 597). In Crocker's case two nodules in the affected part of the scrotum presented the structure of a carcinoma, arising probably in one of the cutaneous appendages.

Carcinoma of the scrotum tends to early invasion of the superficial inguinal glands, the free removal of which, whether enlarged or not, must always be regarded as an essential part of the operative treatment. Unless the primary growth is at some distance from the raphē, the glands of both groins should be removed. Recurrent

carcinoma in the inguinal glands is particularly serious on account of its tendency to extend to those which lie along the main vessels above Poupart's ligament.

In several recorded cases carcinoma has occurred in the groin-glands of chimney-sweeps in whom no primary growth on the scrotum could be detected, and Butlin has suggested, as the most likely explanation, that a small growth on the scrotum, after invading the lymphatics, has itself undergone involution. A similar possible occurrence in the case of the lip has already been mentioned (p. 559). Closely allied to the carcinoma of the scrotum resulting from the irritation of soot is that which occurs in workers in pitch and paraffin, to which attention was first called by Volkmann in 1875 (p. 557).

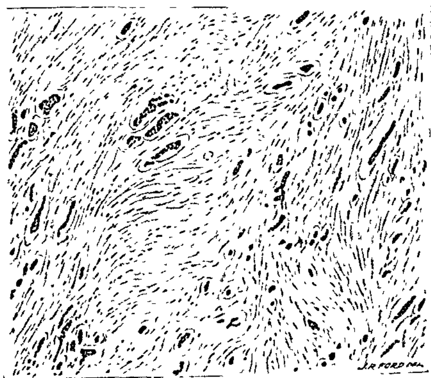


Fig. 153.—Microscopic section of *spheroidal-cell carcinoma of breast* (hard variety).

Carcinoma of the breast.—Although squamous-cell carcinoma occasionally arises in the cutaneous covering of the breast, and columnar carcinoma may originate in the ducts, the ordinary *form* of cancer of the breast is the spheroidal- or polyhedral-cell carcinoma. It is unnecessary to describe the general histological character of the tumour, which has largely served as the basis for the general *descrip-*

tion (p. 546). It is, however, necessary to mention that in their minute structure tumours of the same macroscopic appearance may differ widely, and that great differences may be observed in different parts of the same tumour. The most typical appearances are those seen in Figs. 153 and 154, in which solid columns of epithelial cells, differing only in size, ramify irregularly in a fibrous stroma of very



Fig. 154.—Microscopic section of spheroidal-cell carcinoma of breast (soft variety).

varying amount. Another appearance frequently observed is that illustrated in Fig. 155, in which the malignant epithelium surrounds a lumen and is contained within a definite gland space. Lenthal Cheatle, whose work on the histology of carcinoma of the breast is so well known and who has studied the disease in large serial sections, has shown that this appearance is due to the proliferated epithelium in the small ducts. An earlier stage in the same change is probably seen in Fig. 156.

Precancerous conditions.—In view of the great frequency of cancer of the breast, it is not surprising that many investigators have sought for evidence of pathological conditions in the gland which might prove to stand in a causal relation to the malignant growth. The question chiefly discussed has been the relation between carcinoma

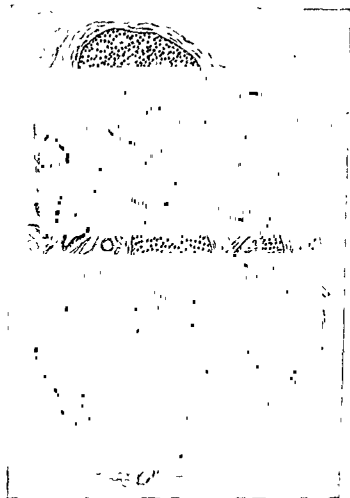


Fig. 155.—Microscopic section of spheroidal-cell carcinoma (duct type) of breast.

and pre-existing chronic mastitis. Clinical evidence on this point is not very trustworthy, but not infrequently suggests that the carcinoma has originated in a part of the gland already the seat of changes due to chronic inflammation. The microscopic evidence is more suggestive, and the signs of chronic mastitis, often with cyst-formation, are often found in close association with carcinoma.

The transformation of a simple glandular tumour (fibro-adenoma) into a carcinoma has often been assumed on altogether insufficient grounds to be a not uncommon occurrence We have already stated our belief that such an origin of carcinoma of the breast is extremely rare; although an adenoma and a carcinoma may lie in close apposition, there is but a single recorded instance in which a malig-

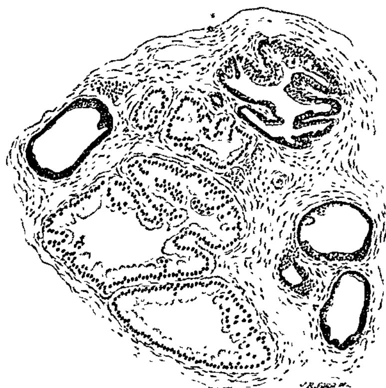


Fig. 156.—Microscopic section from a breast the seat of a spheroidal-cell carcinoma, showing an early stage in the proliferation of the duct epithelium.

nant tumour has been so intimately connected with an adenoma as to suggest its origin from the latter (*see* Vol. II., p. 54).

Paget's disease of the nipple.—In 1874 Sir James Paget described a peculiar form of dermatitis of the nipple and areola, having a superficial resemblance to a circumscribed patch of very chronic eczema, and which he clearly proved to have a close relation with carcinoma of the breast. Beginning at the nipple, the dermatitis slowly spreads centrifugally over the areola, and even beyond it, so that *eventually a patch several inches in diameter may result.* The surface of the skin is red and excoriated, and the seat of small crusts

resulting from the dried serous discharge. Scattered over the reddened surface are often seen small white or bluish-white islands in which the cuticle has not been entirely shed. The skin is slightly thickened, and the margin of the affected patch is sharply defined. The nipple, as a rule, becomes gradually retracted, and its surface may be ulcerated. In many cases, when the patient first comes under observation, a tumour having the features of a carcinoma is already present in the breast. Microscopic examination of the skin in the affected area shows that the earliest change consists in enlargement and round-cell infiltration of the papillæ with swelling of the surface epithelium and

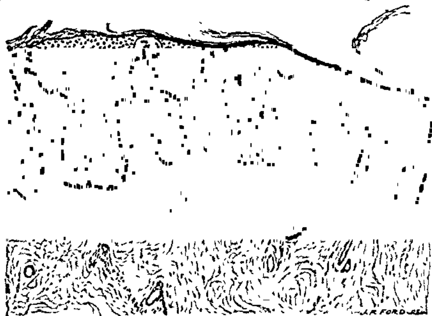


Fig. 157.—Microscopic section of skin of a breast affected with Paget's disease. The breast was the seat of a carcinoma.

interpapillary processes. (Fig. 157.) The horny layer then desquamates, and in the central most advanced parts of the patch the papillæ and interpapillary processes undergo atrophy and the surface epithelium may be reduced to a layer only a few cells in thickness. The large ducts in and beneath the nipple are seen to be blocked with masses of epithelium. Many investigators have studied this remarkable affection with a view to determining the relation in which it stands to the development of carcinoma That the connexion is a very intimate one is certain, and was well shown by the 36 cases collected by Bowlby in 1891, in which a cancer of the breast was present in 25.

Whilst some observers have regarded Paget's disease as a precancerous condition, others consider it to be the result and not the

cause of a carcinoma of the breast. In favour of the former view is the chronicity of the dermatitis, which in one of Bowlby's cases had existed for twenty years without the development of a recognizable tumour, whilst in another in which carcinoma was present the duration of the affection before operation was twelve years. Evidence of this kind is, however, not conclusive, and the only proof that a carcinoma is not present is that afforded by a complete microscopic examination.

In speaking of the various precancerous conditions related to squamous-cell carcinoma, mention has been made of other situations in which a dermatitis apparently identical with Paget's disease of the nipple has been observed; for instance, the skin of the neck, abdominal wall, scrotum, and glans penis. It is interesting to note that in a case of Sheild's, investigated by Rolleston and Hunt, the dermatitis of the mammary region began around the sinus left by an abscess of the breast, and the fungating growth which developed was a squamous-cell carcinoma of somewhat unusual structure. Sampson Handley's recent work on the subject suggests that the dermatitis is the result of an already present carcinoma, and that it is due to permeation by cancer cells of the lymphatics of the subareolar plexus. According to this view, the changes in the papillæ and epithelium are secondary to the lymphatic obstruction, and the blocking of the ducts by the shed epithelium is similarly explained.

In a case of very early Paget's disease which we have recently examined, the skin showed hypertrophy of the interpapillary processes and marked leucocytic infiltration of the corium. The duct epithelium revealed unmistakable evidence of a carcinomatous change, and consisted of large irregular cells arranged in many layers, in some places forming papillary outgrowths. Around some of the ducts was a leucocytic infiltration resembling that in the corium. Between the ducts and beneath the nipple there was considerable fibrosis, but there was no evidence of lymphatic invasion. The condition found in this specimen does not support the view that the changes in the skin and ducts are secondary to lymphatic obstruction, as Handley believes (*see* Vol. II., p. 137), but rather suggests that the cancerous change supervenes on some form of chronic inflammation, involving the nipple and its surface.

The most common type of cancer of the breast is the **nodular hard form of spheroidal-cell carcinoma.** The tumour usually presents itself as a comparatively small, hard lump in the substance of the breast, and its macroscopic characters are best studied in a section made cleanly through the breast in such a way as to pass through the nipple and the tumour. As the knife passes through the latter it encounters a resistant hardness, and a peculiar creak-

ing or gritty sensation is felt, like that felt in cutting through an unripe pear. The divided surface of the tumour is slightly concave or cupped, and, if scraped with the back of the knife, yields a milky juice consisting of epithelial cells displaced from the tumour. In colour the tumour is grey, and less opaque than the surrounding tissue, and is often marked by fine spots and streaks of a yellowish-white colour (Plate 34). These are caused by the larger columns of epithelial cells, and not, at least not solely, by the presence of ducts blocked by proliferated epithelium, for the same appearance is often seen in the secondary deposits in the lymphatic glands. The tumour is thus clearly distinguished from the surrounding opaque white breast tissue or yellow fat. The margin of the growth is well defined, although inseparably continuous with the surrounding tissues into which pointed processes of the tumour often extend. A marked feature of this form of carcinoma is its tendency to shrink and thus exert traction on the surrounding tissues.

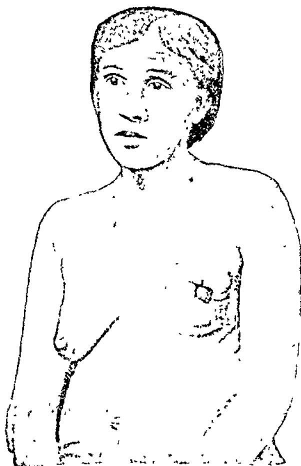
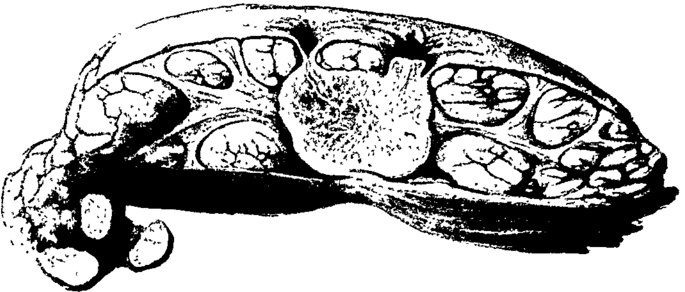


Fig. 168.—Carcinoma of breast, showing results of the shrinking of a hard tumour.

This is often seen, in such a section as is being described, by its effects on the nipple, the skin, and the pectoral fascia and muscle. Unless the tumour is situated peripherally, some of the larger ducts will be seen in the section passing between the growth and the nipple, and by traction on these the nipple is gradually drawn inwards towards the tumour so that eventually it may be deeply retracted beneath the level of the skin (Plate 34). Similarly, the fibrous



Carcinoma of breast.

PLATE 34.

bands (suspensory ligaments) which pass through the subcutaneous fat from the breast to the skin are drawn upon by the shrinking tumour, so that at first the skin is loosely held to the surface of the latter, whilst later it becomes permanently dimpled or puckered, and finally adherent to the growth beneath it (Plate 34). Examination of the deep surface of the tumour will frequently show that the fascia covering this aspect of the breast is adherent to the growth, and at a later stage the superficial fibres of the pectoral muscle are adherent, or even drawn into its substance (Plate 34). This adhesion of the tumour to the fascia and muscle is recognized clinically by the diminished mobility of the breast caused by voluntary contraction of the muscle. Another striking result of the shrinkage caused by a hard carcinoma in the substance of the breast is that the whole gland often becomes less pendulous and the nipple occupies a higher position than the opposite one (Fig. 158).

In extreme cases of atrophic carcinoma the tumour may be scarcely palpable, but even then the shrinking of the breast, the deep retraction of the nipple, and the puckering of the skin afford an unmistakable clinical picture.

The invasion of the skin and the subsequent ulceration of the tumour begin by increasing adhesion of the skin to the surface of the tumour. The skin thus becomes thickened and coarse-looking, and often presents a finely-pitted surface (*peau d'orange*) due to lymphatic œdema. Later a patch of dusky reddish discoloration slowly appears in the centre of the adherent area, and subsequently a small, dry crust forms, on separating which a superficial ulcer is exposed that gradually extends until it assumes the features characterizing the typical carcinomatous ulcer, as already described (p. 548). In this way a huge foul mass of fungating growth may eventually involve a large part of the front of the chest (Fig. 159). When ulceration occurs in a typical atrophic carcinoma the appearance produced may be most striking—a small ulcer firmly adherent to the chest wall being *surrounded by deep radiating puckers in the skin, while the breast* itself has entirely disappeared. Such a growth may pursue a course extending over many years, and be attended with strikingly little impairment of the general health.

The clinical features of a nodular cancer of the breast may be greatly modified by alterations in the skin covering the gland, as the result of lymphatic invasion. Occasionally the skin over the whole breast presents a condition of solid œdema without discoloration. This is a serious sign, and indicates a widely spread lymphatic permeation, even though the palpable tumour is small and circumscribed. Fig. 104 (p. 487) shows the presence of a column of cancer cells in a lymphatic of the skin in a case of this kind. In other cases multiple nodules

of growth are present in the skin of the mammary region, or the skin over a considerable part of the chest may be transformed into a dense indurated layer, constituting the condition sometimes called scirrhus *en cuirasse.* In advanced cases of breast cancer the obstruction may involve the lymphatics draining the upper limb. The whole limb

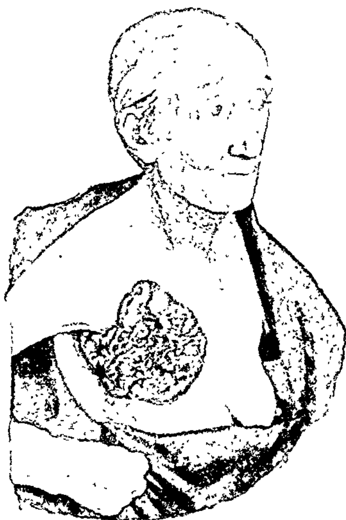


Fig. 159.—*Ulcerating carcinoma of breast.*

may thus become enormously enlarged by a peculiarly dense brawny form of œdema, producing a very distressing condition known as the "brawny arm of cancer."

The mode and routes of the *lymphatic invasion of cancer of the breast* have been very fully studied by many observers not only in their bearing upon the operative treatment of the disease, but also

in relation to the general subject of the spread of carcinoma. The lymphatics of the mammary gland join for the most part in a plexus beneath the areola from which the large efferent vessels pass to the axilla, chiefly to glands which lie on the inner wall of the upper part of the space. Although these glands are usually the first to be invaded by the growth, none of the axillary glands are exempt, and those which lie along the great vessels, as well as those on the posterior wall, are often involved, so that it is essential that in every complete operation the tissue filling the whole space should be removed as thoroughly as possible. Of the lymphatics passing in other directions may be mentioned those which have been found to enter directly the glands lying on the axillary vessels immediately below the clavicle, others passing through the intercostal spaces to the internal mammary chain of glands, and lastly, lymphatics from the inner border of the breast have been demonstrated to pass to the axilla of the opposite side. All these are important in relation to the spread of cancer of the breast. and serve to explain, for example, cases in which the disease involves the glands in the posterior triangle independently of the axillary glands, and also those very rare instances in which a carcinoma of one breast causes secondary deposits in the glands of the opposite axilla.

In 1889 Heidenhain published some very important observations on the mode of spread of carcinoma of the breast in relation to local recurrence of the disease after operation. He showed that in cases of nodular carcinoma, even in the early stages, it was often possible to demonstrate small deposits of growth in the lymphatics of the fascia over the pectoralis major, and further proved that this fascia could only be completely removed by taking away the superficial layer at least of the muscle itself.

The complete removal of the breast in all cases is now universally considered to be essential, on the ground that unless this is done deposits of the growth may be left in the lymphatics of the remaining portion. *The importance of this was emphasized especially by Stiles* of Edinburgh, in his important work on the subject. Again, the complete removal of the breast involves the removal also of the skin covering the gland, for, especially where the suspensory ligaments pass from the surface of the breast to the skin, the breast tissue runs up so close to the latter that if flaps are turned from the breast small portions of the superficial part of the gland are certain to escape removal. Lastly, it will be recalled that Sampson Handley's observations suggest that the disease is especially liable to spread to the abdominal cavity by way of the fascial structures of the epigastrium. These various considerations serve to indicate the extensive nature of the operation which should be performed for even an early localized carcinomatous tumour of the breast. The parts removed should

include the whole breast, with the skin covering it, the sternal and costal portions of the pectoralis major, the pectoralis minor, the fascial structures as low as the epigastrium, and the fat, cellular tissue, and lymphatic glands of the axilla. The removal of the pectoral muscles not only ensures the complete excision of the pectoral fascia, but also, by giving free access to the highest part of the axilla, enables the operator *to deal freely with the subclavicular glands which lie on the* first part of the axillary vein. The removal of both muscles also ensures the removal of infected glands which sometimes lie between the muscles. These glands lie in the position of the superior thoracic artery, and have been shown by Rotter to be very liable to invasion by way of lymphatic vessels which pass from the breast through the large pectoral muscle.

Diffuse hard carcinoma differs from the more common nodular form in the absence of a definite circumscribed tumour and the presence of an ill-defined hardness involving a considerable part or even the whole of the breast. In some instances the affected breast is shrunken, the nipple deeply retracted, and the skin puckered and adherent, whilst in other cases the gland is enlarged and conical, and the nipple and skin are less altered. Such differences are dependent *upon the different degrees of atrophy manifested by the tumour.*

Cancer of both breasts is very rare, if those cases are excepted in which in the late stages of dissemination one or more nodules develop in the breast opposite to that in which the primary tumour originated. In considering the question of operation in such cases, the condition of the disease on each side must be separately considered, and if on each side it is favourable for operation, the double operation should be performed.

Soft carcinoma of the breast is not common, and is rarely so soft as to justify the name "encephaloid." Tumours of the breast, as of other parts, which are brain-like in consistence, prove as a rule to *be sarcomas and not carcinomas. The soft form of* cancer usually occurs as a more or less globular tumour in the substance of the breast. The various effects observed as the result of the contraction of a hard, *shrinking carcinoma*, especially upon the skin, nipple, and pectoral muscle, are usually absent or but slightly evident in the softer forms of the disease. The tumour tends to increase rapidly, causing early implication of the *skin and invasion of the* lymphatic glands. The diagnosis [illegible] sarcoma of the breast may be imposs[illegible] examination, and the clinical re[illegible] *uch as cysts* containing papillomatous growths, may be very close.

The soft form of carcinoma of the breast sometimes, especially in young women, assumes a diffuse and *particularly malignant* form,

which, on account of its resemblance to an inflammatory affection of the gland, has been known as "*brawny cancer*" or *carcinomatous mastitis*. The whole breast is enlarged, tender and hot, and the overlying skin reddened and œdematous, or it presents the peculiar *peau d'orange* appearance. In a case of this kind which came under our notice the patient was but 22 years of age, and the disease had only been noticed for a few weeks. In the belief that the enlargement of the breast was due to an abscess, an incision had been made into it. The breast was removed, but recurrence rapidly followed and proved fatal.

Some of the most malignant examples of this form of cancer are met with during pregnancy and lactation, the disease either arising during these periods, or a slowly growing tumour, already present, assuming the characters of the more malignant type. Marmaduke Sheild has collected numerous cases of this nature, one of the most striking being that recorded by Billroth, in which the disease developed in both breasts five weeks before parturition, death occurring a week afterwards with universally distributed secondary deposits.

The malignancy of this form of cancer was strikingly illustrated by a case under the care of Rose Bradford in University College Hos- [illegible] uring lactation on account [illegible] impairment of resonance, [illegible] h lungs. As the breasts diminished in size with the cessation of lactation it was noticed that the left remained larger and harder than the right. Rapid emaciation occurred, and the patient died eighteen days after her admission into the hospital. The left breast was the seat of a diffuse carcinoma, and there were secondary deposits in the lungs and liver and in the axillary, mediastinal, and abdominal lymphatic glands

Colloid carcinoma occurs in the breast as a modification of the ordinary undifferentiated form, but is not common (Fig. 160). The mucoid or colloid change may affect only part of the tumour without modifying its clinical features, and is only detected in a section of the growth by the presence of areas presenting a fine reticulum, the meshes of which are filled with yellowish jelly-like substance. When, however, the colloid change is more marked, the tumour, which is sometimes of slow growth, is usually rounded or lobulated, and moderately soft in consistence. It shows little tendency to contraction, and in exceptional cases may form a prominent elevation of the skin, of a slightly bluish tint, and somewhat resembling a cyst. The secondary growths may or may not present a similar degeneration. Although the malignancy of a carcinoma is probably diminished by colloid changes in the cancer cells, the removal of the disease should be carried out on the same lines as those adopted in the ordinary forms of breast

cancer. We have ourselves seen a case in which a typical colloid carcinoma of the breast was associated with a widespread invasion of the surrounding lymphatics with undegenerated cancer cells. Kelly and *D'Este* Emery have recorded a very remarkable case of carcinoma of the breast in which certain local recurrent growths and metastases exhibited advanced colloid degeneration. The *primary* tumour was regarded as a simple duct papilloma, but subsequent

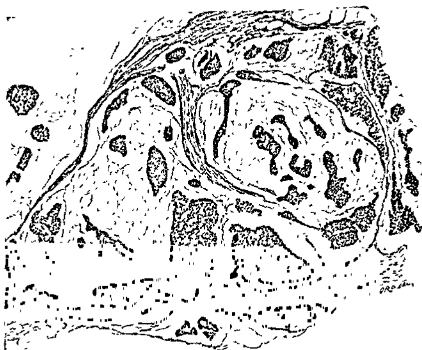


Fig. 160.—Microscopic section of colloid carcinoma of breast. The alveoli are occupied partly by colloid material and partly by the undegenerated remains of cancer cells.

examination revealed the presence of a typical spheroidal-cell growth in the tissue around the cyst. Recurrent growths which were removed six and seven years after the first operation presented marked colloid change. Death occurred seven and a half years after the removal of the primary tumour, and secondary deposits were found in the sternum, skull, lungs, and liver. In the lungs and the sternum the growths were colloid, but in the skull and the liver the deposit presented the usual characters of a spheroidal-cell carcinoma. The deposit in the skull had destroyed a large area of the right half of the frontal bone, the opening being occupied by a thin membrane, and the only evidence of growth being found in the bone immediately surrounding the aperture.

Metastases are extremely common in spheroidal-cell carcinoma of the breast, and the most common sites of the secondary growths, other than the lymphatic glands, are the liver, the lungs, and the bones Among 735 post-mortem examinations tabulated by Stephen Paget, the liver was affected in 241, and the lungs or pleura in 70. Paget found that the ovaries were involved in 37 cases, an interesting fact to which allusion has already been made in discussing Sampson Handley's views on the subject of dissemination of cancer of the breast (p. 492). The frequency of deposits in the bones is a feature shared by cancer of the breast with similar disease in the thyroid gland and prostate, and this subject has also been already briefly considered (p 552) From the statistics of the Middlesex Hospital, Handley finds that the frequency with which the individual bones are affected is—sternum, ribs, femur, spine, cranial bones, humerus, clavicle, whereas among the 329 cases tabulated, the scapula, tibia, patella, and bones of the hand were each only once affected, and the hip-bone, radius, ulna, fibula, and bones of the foot were in no instance involved. As Handley points out, certain fallacies occur in such statistics, on account of the incomplete examination usually made of the skeleton at post-mortem examinations Deposits are thus likely to be overlooked, especially in bones in which spontaneous fracture does not attract attention to the disease. It is, indeed, probable that the spine is more liable to secondary deposits than this list would indicate, and according to von Recklinghausen the order of frequency is—spine, ribs, sternum, femur, and humerus.

One point of clinical importance in connexion with metastases in breast cancer is that they may occasion symptoms of an obscure nature even at an early stage of the disease, when the existence of a tumour of the breast is unsuspected. Osler has drawn special attention to this aspect of the disease, and has pointed out that the symptoms resulting from a secondary deposit may be such as to mislead the physician. Osler mentions, amongst others, the case of a powerfully built man who, after suffering for some months with symptoms of disease of the spinal cord, was admitted to the Johns Hopkins Hospital with paraplegia. The symptoms proved to be the result of deposits of growth in the spine secondary to a carcinoma of the right breast. Similarly the secondary deposits in the thorax may occasion pleurisy of doubtful origin, or symptoms of mediastinal tumour, even when the tumour of the breast is so small as to be either overlooked or disregarded. Murray of Manchester, in association with one of us, has recorded a case in which the nature of certain paralyses and muscular atrophies in the upper limbs was altogether obscure until a small tumour, having the characters of a carcinoma, was accidentally discovered in the breast. The nervous phenomena were subsequently

proved to be caused by a secondary growth in the cervical spine involving certain nerve-roots.

Columnar-cell carcinoma of the breast is comparatively rare, and is usually known as "duct cancer" or "villous cancer." The name "villous cancer," first used by Cornil and Ranvier, is only of limited applicability, for it is not all columnar-cell carcinomas of the

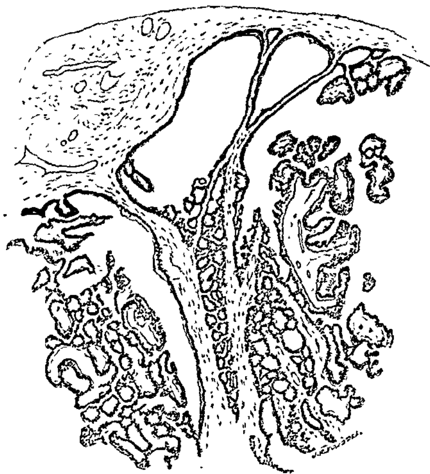


Fig. 161.—Microscopic section of columnar-cell carcinoma of breast.

breast that exhibit a papillary structure. The simple duct papilloma of the breast has already been described (p. 483), and from this benign growth the villous cancer is distinguished by the fact that, instead of remaining as a papillomatous growth in the interior of the duct, the growth originating in the duct epithelium infiltrates the surrounding tissues in the form of spaces filled with villous processes covered with columnar cells. (Fig. 161.) We cannot but conclude that considerable confusion has arisen between these two forms of growth, and that to

a certain extent an exaggerated idea of the comparatively low malignancy of columnar-cell carcinomas of the breast has resulted from including with them certain simple duct papillomas.

A typical columnar-cell carcinoma usually occurs in the central part of the breast as a comparatively soft tumour intimately connected with the breast tissue, and exhibiting little evidence of traction upon the surrounding tissues. A blood-stained discharge from the nipple may be present, and sometimes the tumour is definitely cystic. There is no doubt, even allowing for the probable fallacy above mentioned, that the malignancy of columnar-cell carcinoma is less than that of the common form of cancer of the breast, and metastases are quite exceptional. Godlee has recorded a case in which secondary deposits were present in the axillary glands, and Shattock one in which, although the structure of the breast tumour was not known, a metastasis in a rib presented the typical structure of columnar-cell carcinoma.

Carcinoma of the male breast, although of special interest on account of its comparative rarity, presents no anatomical peculiarities to which reference need be made here.

Carcinoma of the uterus is much more common in the cervix than in the body. In the **cervix** it may begin in the vaginal portion or in the canal When arising in the vaginal portion the tumour may present the characteristic structure of the squamous variety, and when arising in the epithelium of the cervical glands it may retain the columnar type, but in neither case is the character of the epithelium always preserved in the tumour cells, so that the structure is sometimes that of undifferentiated carcinoma; thus, except in its earliest stages, its exact origin may be doubtful. In some forms of cancer of the cervical glands the cells lining the spaces retain a very regular form and arrangement, and show none of the usual heaping-up and proliferation of the columnar epithelium, and the histological resemblance to a simple adenoma is, therefore, so close that the recognition of its malignant nature by the examination of a scraping can hardly be made. A tumour of this structure is sometimes called a malignant adenoma (Fig. 162)

Carcinoma of the vaginal portion occurs either as an ulcer or as a warty growth; as it increases it tends to spread around the cervix, forming a considerable mass, and extending to the vaginal fornix rather than into the cervical canal. Thence it may spread to the base of the broad ligaments, and to the iliac and sacral glands.

Carcinoma of the canal of the cervix may for a considerable time remain confined to the interior, and the os show little change, although later it may become involved in the growth and ulcerated. The growth rarely extends to the body of the uterus, but, like a tumour beginning in the vaginal portion, spreads into the parametrium and

causes similar glandular invasion. The growth is more malignant than cancer of the vaginal portion, and shows a greater tendency to cause metastases, especially in the lungs, viscera, and bones.

A carcinoma of the vaginal portion usually presents itself in its earliest stage as an induration of one lip of the os with a warty or superficially ulcerated surface, whilst in a growth beginning in the canal the os is at first unchanged. Finally, however, in both varieties

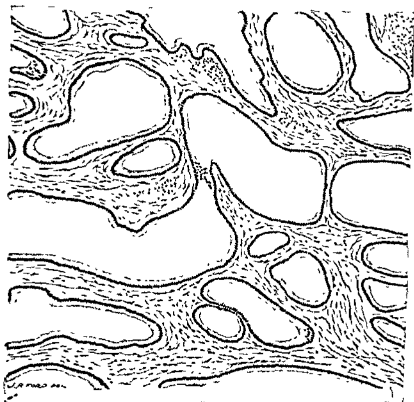


Fig 162.—Microscopic section of columnar-cell carcinoma of cervix uteri (malignant adenoma).

(From a case under the care of Herbert Spencer)

of the disease the whole of the vaginal portion of the cervix may be destroyed by ulceration, so that the origin of the disease cannot be determined either by its clinical or its microscopic features. When the pelvic tissues are involved, the pressure on the ureters and resulting hydronephrosis may be the cause of death, or the disease may spread to the bladder or rectum, sometimes causing fistulous communications.

Carcinoma of the **body** of the uterus is much rarer than carcinoma of the cervix, and, unlike the latter, has no relation to childbirth. It arises in the epithelium of the uterine glands, and in the typical form

the cells retain the columnar shape, but more often this is more or less completely lost and the growth has the structure of spheroidal-cell carcinoma. The tumour usually presents itself as a soft, white, spongy or papillary growth projecting from some part of the inner surface of the uterus. It tends to spread, so that eventually it may involve a considerable part of the uterine wall as a thickening of the lining. In section the growth is seen to be invading the muscle, but a sharp line usually distinguishes the two, and even in the later stages the outer part of the muscular wall and its serous covering remain intact, so that, although considerably enlarged, the uterus may still retain its normal shape. Ultimately, however, the growth may form bosses on the peritoneal surface, and, extending to the parametrium, cause extensive adhesions and nodules on the adjacent peritoneum. Secondary deposits in the lumbar glands are exceptional, but deposits may be found in the ovaries; metastases are rare.

The proliferation of the uterine glands met with in cases of glandular endometritis or hypertrophy may produce appearances very difficult to distinguish histologically from carcinoma. Carcinomas of the body of the uterus in which the cells are of the squamous form have been described, and are supposed to arise in the surface epithelium after it has undergone squamous metaplasia.

Chorion-epithelioma.—Although the rare malignant tumour known by this name is not altogether confined in its origin to the uterus, this is the most convenient place to notice it. It is a special form of carcinoma which originates in the epithelium of the coverings of the embryo or fœtus. The tumour most frequently arises from the placental villi, but may develop after abortion in the early stages of the development of the ovum. Chorion-epithelioma thus usually occurs as a tumour of the uterus, but it has been met with in the Fallopian tube in cases of tubal gestation, and is stated to have arisen occasionally as a primary growth in the wall of the vagina, possibly from the implantation of a fragment of a chorionic villus. Rarely the tumour has been observed to arise in connexion with teratomas of the ovary, mediastinum, and testis, presumably in cells homologous with the surface epithelium of the fœtal membranes.

In its relation to pregnancy, the development of the tumour varies, occurring sometimes after abortion, during pregnancy, shortly after parturition, or even a year or more subsequently. In one-half of the recorded cases hydatidiform mole has preceded the development of the tumour, and it is of interest that in this affection proliferation of the epithelium of the chorionic villi also occurs.

When fully developed a chorion-epithelioma of the uterus forms a soft, blood-coloured, flattened mass on the inner surface, or may appear as a more prominent fungating or lobulated tumour occupying the

placental site (Fig. 163). As the tumour increases it spreads in the wall of the uterus, distending the cavity, and possibly projecting into the cervical canal. On section it presents the appearance of blood-clot, of

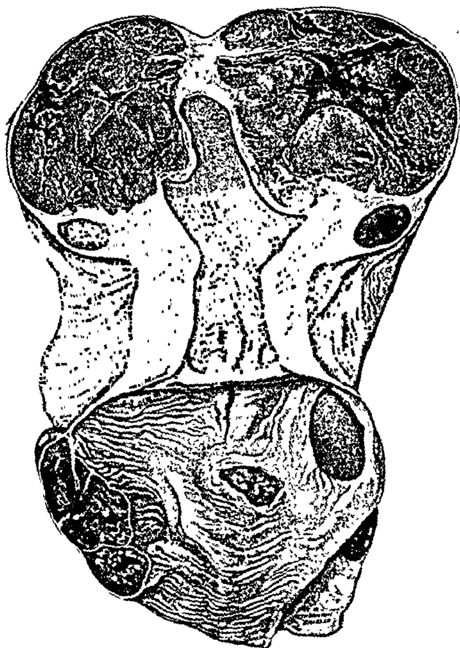


Fig. 163.—Uterus and vagina laid open to display a chorion-epithelioma of body of uterus and a secondary deposit in vaginal wall.

(*From a case under the care of G F Blacker*)

which indeed the mass is largely composed, but at the growing edge of the tumour in the wall of the uterus yellowish-grey areas are seen in which the tumour substance is free from hæmorrhage. Finally, the growth may reach the serous surface of the uterus, where it forms smooth, rounded projections in which the hæmorrhagic appearance of the tumour is visible.

Microscopic features.—In many parts a chorion-epithelioma shows under the microscope little more than blood and necrosed tissue, in which no definite structure is recognizable. Usually in certain areas of the tumour and in a narrow zone at the growing margin a typical



Fig. 164.—Microscopic section of a chorion-epithelioma of uterus, showing plasmodial masses with vacuoles containing nucleated cells with clear protoplasm.

and very characteristic structure can be observed (Fig. 164), consisting of the following elements: 1. Plasmodial masses of deeply staining protoplasm (syncytium), in which no indications of cell boundaries can be recognized, but which contain large numbers of irregularly scattered or more closely aggregated nuclei. In some parts the protoplasmic masses, instead of being continuous, are vacuolated by large, rounded, oval, or irregular spaces, producing the appearance of a large-mesh network of protoplasmic strands. 2. Filling the spaces in the plasmodium are masses of small, rounded or polygonal cells of very uniform appearance. The cells are closely packed, have a very distinct dark boundary line, a clear non-granular protoplasm, and a deeply

staining nucleus. 3. A large intermixture of blood and blood-clot. Rarely, in parts of a tumour the structure of a hydatidiform mole is reproduced, the cells being arranged so as to give rise to a vesicular structure. This occurs not only in uterine tumours, but also in those occurring in other situations, such as the testis.

Of the two epithelial layers of the chorionic villus, the outer or syncytial layer gives rise to the plasmodial masses, while the deep or Langhans' layer is represented by the masses of small, clear cells.

In some cases, especially in the metastatic growths, the structure is less typical than that above described. Thus, the plasmodial masses may be imperfectly formed, consisting either of isolated masses of non-vacuolated protoplasm containing two or three nuclei, or being replaced by large angular cells with deeply staining protoplasm and nucleus.

The tumour cells are strongly attracted towards the veins of the tissue which they infiltrate, and often form a layer beneath the endothelium, or a complete tube around it. As a result of destruction of the endothelium, blood passes freely into the tumour substance, breaking up the growth and causing extensive necrosis. The regional lymphatic glands are liable to invasion, and secondary deposits are also common in the vagina (Fig. 163) and vulva.

Owing to the extension of the tumour cells into the veins, metastases by way of the blood-stream are very frequent. They are most common in the lungs, but have also been met with in other parts such as the brain, kidneys, and subcutaneous tissue. In these parts the metastases form rounded nodules, usually varying in size from a pea to a walnut, and on section present a marbled red and yellowish-grey appearance owing to the presence of hæmorrhages. It is stated that after removal of the primary tumour the metastases have occasionally retrogressed and disappeared. In cases of chorion-epithelioma the ovaries have usually been found to be somewhat enlarged owing to the abundant production of lutein tissue, taking the form of luteal cysts.

Carcinoma of the ovary is not uncommon, and may probably originate in the germinal epithelium or in the epithelium of a Graafian follicle. Histologically the tumour may present alveoli lined with cubical or columnar cells or masses of cells, or it may have a spheroidal-cell structure. Macroscopically, it may occur as a soft, solid tumour, sometimes of large size, smooth or slightly lobulated, and often retaining the form of the ovary. In other cases the tumour may present itself as a multilocular cyst, which to the naked eye presents no evidence of malignancy, or in which, on section, solid masses are seen between the cysts or in their walls, or projecting into the cysts so as partly or completely to fill them. The solid growths may rupture through the cyst wall, and appear as outgrowths on the surface of the cystic tumour. Carcinoma of

the ovary, in either the solid or the cystic form, is sometimes bilateral. Secondary deposits in the pelvic lymphatic glands and peritoneum and metastases elsewhere may occur. It is very important to remember, as has already been pointed out, that secondary carcinoma of the ovaries, sometimes bilateral, is not very uncommon, especially when the primary growth is situated in the breast, stomach, or other abdominal viscera Bland-Sutton, who doubts the existence of primary cancer of the ovaries, has called especial attention to the fact that sometimes the existence of the primary growth may be overlooked and the secondary deposit in the ovary regarded as primary. The same observer has also pointed out that secondary carcinoma may occur in an ovary which is already cystic.

Carcinoma of the Fallopian tube is rare, and usually occurs as a fungating mass distending the tube.

Carcinoma of the vagina is not common; it generally assumes the squamous-cell form, and may commence as a warty growth or ulcer In advanced cases the disease may extend to the rectum or bladder, and fistulous communications result.

Carcinoma of the vulva is not very frequent, and presents no features requiring special description. It is very constantly associated with a precancerous condition of the part, which was first described by Morris, who pointed out its similarity to the corresponding condition of the tongue. This condition is known as "leucoplakic vulvitis." Comyns Berkeley and Victor Bonney have carefully described the affection and the histological changes present in its different stages. The whole of the vulva, with the exception of the vestibule and urethral orifice, is liable to be involved, and the changes may even spread to the folds of the thighs and to the perineum. The affected parts, at first red, swollen, and excoriated, next become white, shrunken, and thickened, and later the seat of cracks and ulcers. Finally, unless carcinoma has supervened, the whole vulva becomes smooth, shiny and white, the labia minora and clitoris practically disappear, and the disease becomes quiescent. It is from the ulcers and fissures that carcinoma is especially liable to arise, but it may develop at an early stage from the enlarged and branched interpapillary processes of the epithelium Berkeley and Bonney state that in every case of carcinoma of the vulva which they have seen, leucoplakic vulvitis has been present. The same observers point out that the condition known as kraurosis vulvæ, which is characterized by an atrophic condition of the vulva, with stenosis of the vaginal orifice, is an essentially different affection, and stands in no causal relation to carcinoma.

Multiple carcinomas of the vulva have already been mentioned as a possible example of auto-inoculation, and the view expressed that such growths are more probably due to independent developments

in a part already in a precancerous condition. The lymphatic glands liable to be involved by the disease belong to the superficial inguinal group.

Operative treatment should include the removal not only of the actual growth, but also of those parts presenting the precancerous changes, as well as the glands, whether enlarged or not, of both groins.

MIXED TUMOURS

TERATOMA

Already in considering the different varieties of tumours we have seen that in many instances more than one form of tissue enters into their structure, and that not only may different forms of connective tissue occur, as, for instance, in such growths as angio-lipoma and chondro-sarcoma, but even epithelial and connective-tissue elements may be associated, as in the papillomas and adenomas. There remain, however, certain tumours, frequently of a more complex structure, and containing different tissues often highly differentiated and irregularly arranged, which require separate consideration. Among such tumours the most complex are characterized by the fact that the component tissues are so arranged as to produce a more or less striking resemblance to definite fœtal structures, whilst other tumours occur which are clearly of a similar nature but in which the component tissues present no tendency to be grouped in such a way. Tumours of the first variety are sometimes called *teratomas*, and those of the second variety *teratoid*, but it seems more convenient to apply the name teratoma to the whole group. It is a feature common to all members of this class that tissues derived from all the three layers of the blastoderm are present, although one or another layer may be chiefly represented. Mixed tumours of this nature are supposed to arise in one of the following ways:—

1. In cases of partial or complete duplication of the embryonic area it is supposed that one portion may continue its normal process of development into an individual, while the other portion fails to undergo immediate development, and, becoming included within the body of the former, subsequently gives rise to a mixed tumour (fœtal inclusion). According to this view the process is closely allied to that by which the various forms of double monster are produced, but in this case the part of the divided embryonic area, which in the other instance forms the tumour, develops into an attached individual or part of an individual.

2. Another possible mode of formation, which can, however, only be applied to tumours of the ovary and testicle, is that they arise by

the spontaneous development of a germinal cell. Among the various views which have been advanced in this connexion is that which supposes the process to be analogous to parthenogenesis (the development of an unfertilized ovum) as observed in some of the lower animals, while Shattock suggests that a tumour may result from an ovum fertilized by a spermatozoon included in the ovary during the process of its development.

3. During the segmentation of the ovum after fertilization it is supposed that one of the blastomeres may become displaced, and that, remaining included in some part of the body, it develops subsequently into a tumour.

4. Lastly, it is probable that mixed tumours may in some instances arise as a result of local developmental errors, such as duplication or the delayed growth of a portion of undifferentiated tissue in situations where the different blastodermic layers come into juxtaposition. Thus, duplication of the mandible has been supposed to account for certain tumours in the neck, whilst it is possible that some mixed tumours of the testicle may arise in tissue which has become embedded in the organ during the early stages of its development and brought down with it during its descent.

From what has been said, it is evident that mixed tumours of this class must differ very widely in their clinical characters and in their structure. It is thus impossible to give any general description of them, and it must suffice to describe the chief characters that they present in the most important situations in which they occur. It may, however, be mentioned that although in many instances they behave as benign growths, it is not rare, especially in certain situations, to find a tumour evidently of this nature exhibiting evidences of malignancy. Such a malignant change may occur in the epithelial or in the connective-tissue elements, and thus the resulting growth may behave as a carcinoma or as a sarcoma, whilst occasionally the extensions of the growth reproduce to a varying extent the complex structure of the primary tumour.

Teratoma of the ovary usually occurs as the well-known *ovarian dermoid*. In its most simple form this consists of a cyst lined with skin, furnished with hairs and other cutaneous appendages such as sebaceous glands, and filled with fatty material often containing cholesterin. In its most complex form the ovarian dermoid consists of a simple skin-lined cyst from the inner surface of which projects a complicated mass having sometimes a close resemblance to a fœtus. Between these two extremes every gradation occurs, the most common being that in which a prominent nipple-like projection is present, bearing hairs on its surface, and various tissues, such as bone, cartilage, teeth, epithelial tubes, or nerve elements, in its

substance. These tumours never attain the enormous proportions of the ovarian cyst-adenoma. They are most common in early adult life, but have been found in children even as early as the third year. The tumours may be bilateral, and more than one may be present in the same ovary, and, like other ovarian cysts, they are liable to torsion of the pedicle. Occasionally an ovarian dermoid acquires secondary attachments to some other part, such as the omentum, so that its true origin is rendered obscure. A malignant change in an ovarian dermoid is usually evidenced by the presence of *a warty mass on its inner surface.*

Closely allied to, but much more rare than, the ovarian dermoid are certain solid tumours of the ovary which usually, if not always, pursue a malignant course and are described as "*malignant embryoma*" In one of two cases of this nature recorded by Targett and Hicks, the tumour, which had undergone torsion of the pedicle, was removed by operation from a girl aged 14 years. Five months later a large recurrent growth was present in the left iliac fossa, and sessile and pedunculated growths were studded over the intestines and omentum. Ascites was present, and recurred after repeated tappings, and death ensued seven months after the first operation The peritoneal growths were very extensive, and some of the masses had probably originated in the retroperitoneal glands The primary and secondary growths presented on microscopic examination tubules and cysts *lined with columnar or stratified epithelium, nodules of cartilage* and bone, epithelial pearls, and a stroma of fibrous, muscular and fatty tissues, with groups of ganglion cells, but no resemblance to any definite organ could be traced. Among the thirteen recorded cases collected by Targett and Hicks, eleven were undoubtedly malignant, and of these nine died within a year. The ages varied between 6 and 30 years. The metastases are chiefly in the peritoneum and retroperitoneal glands, whilst in the viscera they are rare. In some cases, as in that above described, the secondary deposits have the same complex structure as the primary tumour, but in others they present the structure of a small round-cell sarcoma.

Teratoma of the testicle.—In the testicle, as in the ovary, two forms of teratoma occur, the dermoid, and the solid tumour of composite structure in which cysts are almost invariably recognizable even with the naked eye; but whereas in the ovary the dermoid is much more common than the solid form, in the testicle the reverse is the case and dermoids are extremely rare. On account of the complex *structure of the solid teratomas* they have received many different names, such as cystic disease of the testicle, adenoma testis, chondrosarcoma, and columnar carcinoma. A consideration of the structure of *these tumours readily explains how such a complicated* nomen-

clature has arisen, and it is better to include them all under the general name "teratoma" rather than to name each specimen according to its naked-eye or histological features.

The solid teratoma or embryoma presents itself clinically, usually in young adults, as a tumour causing an apparently uniform enlargement of the testicle, or, if the cystic formation is marked, the

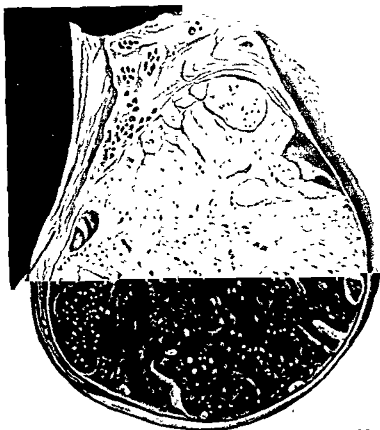


Fig. 165.—Teratoma of testicle.

tumour may be lobulated and in parts elastic. Dissection shows that the tumour is contained within the tunica albuginea, and between the two it is sometimes possible to demonstrate the testicular substance spread out in a thin layer, while the epididymis can sometimes be recognized behind the tumour. The tumour itself presents on section differences dependent chiefly on the extent of the cystic formation. Sometimes it is a soft solid growth in which minute cysts are visible (Fig. 165), sometimes it has the appearance of a coarse sponge-

work; or a few large cysts may be associated with a varying amount of solid substance. In the latter, gelatinous areas are sometimes visible, and cartilage may be present in the form of white or greyish nodules. Occasionally the cysts contain intracystic growths.

Among the elements most easily *demonstrated microscopically* in these mixed tumours are the connective-tissue stroma, which varies

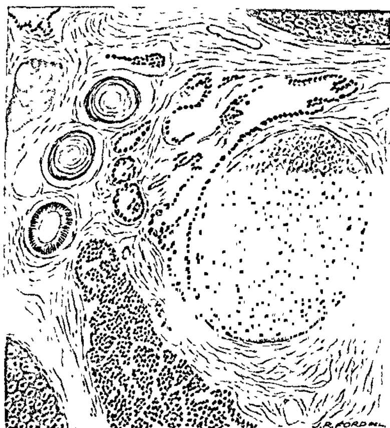


Fig. 166.—Microscopic section of teratoma of testicle, showing connective-tissue stroma containing cartilage and spaces lined with columnar and cubical epithelium, and two masses of stratified epithelium.

widely in its character and often contains cartilage, and spaces lined with cubical or columnar epithelium. Other elements can, however, always be found, and Nicholson, who has recorded the results of his examination of sixteen specimens, most of which are in the Museum of Guy's Hospital, has been able to show that derivatives of all the three layers of the blastoderm are present. The epiblast is represented by tubules *lined with stratified epithelium and epithelial pearls*; the mesoblast by the connective tissue, often with cartilage, some-

times with muscle or even bone; and the hypoblast by the columnar or cubical epithelium, which is often arranged in the shape of villi and surrounded by unstriped muscle (Fig. 166). The origin of these tumours has been the source of much discussion and must be regarded as still uncertain. After reviewing the various theories, Nicholson concludes that the most probable explanation is that first suggested by Wilms, who supposes that they arise in the reproductive cells themselves, by a process analogous to parthenogenesis. Although the solid teratoma of the testicle may pursue a benign course, occasionally, like the corresponding tumour of the ovary, it undergoes a malignant change, and may thus probably behave as a carcinoma or as a sarcoma. In a case recorded by Horsley in the *Transactions of the Pathological Society*, the secondary tumours in the lungs and liver were purely sarcomatous, although the primary growth in the testicle contained spaces lined with columnar epithelium.

As an example of a teratoma of the testicle producing metastases of complex structure may be mentioned the classical case described by Paget in 1855 as a malignant enchondroma, in which the cartilaginous growth reached the vena cava by way of the spermatic veins and caused metastases in the lungs. Subsequent examination of the specimens from this case led Kanthack and Strangeways to regard it as a columnar-cell carcinoma with cartilaginous formation in the stroma, but still more recently the discovery of epithelial pearls in certain of the nodules of growth by Nicholson seems to complete the evidence that the tumour is in reality a teratoma. The metastases in the lungs containing cartilage and spaces lined with columnar epithelium must be regarded rather as the result of the transplantation of fragments of the growth which reached the interior of the vena cava than as an evidence of any true malignant change in the cells of the tumour.

In rare instances a tumour having in part the structure of *chorion-epithelioma* (p. 611) occurs in the testicle. Such a tumour, as first pointed out by Schlagenhaufer, must be regarded as a teratoma in which the chorio-epitheliomatous growth has arisen from the epiblast. In a specimen of this nature which we have examined the tumour contained, in addition to syncytial tissue, islands of hyaline cartilage and tubules lined with cylindrical epithelium. The presence of this modification in the structure of a testicular teratoma is likely to be associated with extensive hæmorrhagic extravasations, which may, to a large extent, obscure the nature of the growth. In more than one recorded case the tumour has contained villi resembling those of a vesicular mole. These tumours are usually very malignant and tend to cause metastases through the blood-stream. Among four cases described by Nicholson, there were metastases in the lungs and brain

in one, in the abdomen in another, and in the liver, abdominal glands, and lungs in a third.

Dermoids (cystic embryomas) of the testicle are very rare, and are distinguished from simple dermoid cysts of the scrotum by the fact that they are contained within the tunica albuginea. As in the ovarian dermoid, a process of complex structure may project into the cyst. In a tumour of the testicle described by Barrington, a dermoid cyst, lined with stratified epithelium and provided with sebaceous and sweat-glands, was associated with a solid tumour having the histological structure of a carcinoma with columnar and irregular cell-elements. It is probable that in this case the carcinomatous growth originated in the hypoblastic element of a teratoma, the epiblastic element of which was represented by the dermoid cyst

Teratomas of the cranium and spine are classified by Borst according as they are or are not associated with crania or spina bifida. In the cranium they have been met with on the convexity or at the base. As an example of the extraordinary features which such a tumour may present at the base of the skull may be mentioned the specimen described by Breslau and Rindfleisch, and cited by Borst, in which a pedunculated tumour projecting into the pharynx was connected through a hole in the floor of the sella turcica with an intracranial tumour which presented seven rudimentary limb-like projections, and contained, amongst other structures, cartilage, bone, muscle, nerve, intestine, and renal tissue.

In connexion with the spine, teratoma is chiefly met with at the lower extremity as the **congenital sacro-coccygeal tumour.** This is usually situated on the anterior aspect of the sacrum and coccyx, between them and the rectum. It may reach a large size and project downwards between the lower extremities. The tumour is usually partly cystic and partly solid

Among the histological elements found in such tumours may be mentioned various forms of connective tissue, often including cartilage, and spaces lined with columnar or, less commonly, stratified epithelium. In view of the complex structure of these tumours and the fact that derivatives of all the three blastodermic layers may be present, it is probable that they are rightly regarded as teratomas. It must, however, be mentioned that this view is not generally accepted, different pathologists having assigned their origin to the neurenteric canal, postanal gut, or Luschka's coccygeal gland.

Morley Fletcher and Waring have recorded a case of sacro-coccygeal tumour which exhibited malignancy. The tumour was removed from a child 2 years of age, who died with extensive recurrence in the pelvis three and a half months after the operation. There were also masses of growth in the lumbar and iliac glands The primary tumour

was partly cystic and partly solid. The cysts were lined with columnar epithelium, and the solid part of the growth, as well as the deposits in the glands, had the structure of an "adeno-carcinoma."

Closely allied to the congenital sacro-coccygeal tumours are the dermoid cysts which have occasionally been found between the sacrum and the rectum

Teratomas of other parts of the spine are exceedingly rare. We have described a specimen in the *Proceedings of the Royal Society of Medicine*, in which a large teratoma, situated behind the peritoneum

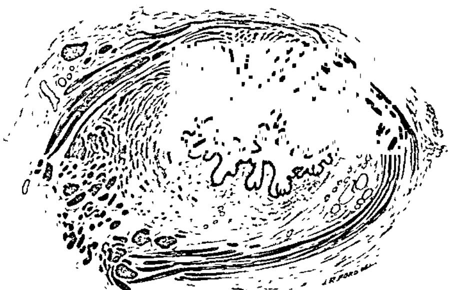


Fig. 167.—Microscopic section of part of a teratoma of the spinal column, showing a branching space lined with columnar epithelium and surrounded by unstriped muscular tissue.

in the left renal region, was very intimately connected with the spinal column, and actually projected into the spinal canal (Fig. 167).

Reference may here be made to another form of growth which has been met with in the sacro-coccygeal region, and to which the name *chordoma* has been applied. It is believed to arise from the notochord, and has more commonly been encountered in the region of the spheno-occipital synchondrosis Stewart of Leeds, who has recently reviewed the literature of the subject, states that "the tumour is alveolar in structure, and the parenchyma, usually of epithelial type, is composed of cells which become the seat of mucoid degeneration at a very early stage of their development." In most of the recorded cases of chordoma the tumour has pursued a malignant

course. Thus, in the case studied by Stewart, the primary tumour projected backwards from the sacro-coccygeal region, and secondary deposits subsequently occurred in the left buttock, over the right scapula, and in the scar resulting from the removal of the primary growth.

Teratoma of the thorax.—A considerable number of cases are on record in which a teratoma, usually in the form of a *dermoid* cyst, has been present in the thorax, the tumour being situated in the mediastinum, lung, or pericardium. The effects which may result from such a tumour were well illustrated by Godlee's case, in which a *right-sided pleurisy, followed by empyema, was the first striking evidence* of serious disease. Later the empyema ruptured into a bronchus, and, as in other recorded cases, hairs were present in the expectoration. By operation a cavity filled with hair and fatty material was opened; the cavity was lined with skin, and three fleshy masses bearing hairs on their surface projected into it. The cavity remained open, and *the patient died about three years later of some septic complication.*

In a case recorded by Ritchie a mediastinal teratoma occurring in the male presented in part the structure of chorion-epithelioma, and nodules which were present in the lungs showed the same structure.

Teratoma of the abdomen.—Apart from the teratomas which originate in the genital organs and those occurring in the retroperitoneal tissue, tumours of a similar nature and probably arising from fœtal inclusion have been described in various parts of the abdominal cavity, such as the region of the liver, the transverse mesocolon, and beneath the diaphragm.

Teratoma of the neck.—A congenital tumour is occasionally met with in the neck which closely resembles the sacro-coccygeal tumours above described. Of four specimens in the Museum of the Royal College of Surgeons, three are median, but in the fourth a tumour extends from the left side of the neck upwards under the ascending ramus of the jaw, *causing great deformity and compressing* the brain. According to Keith, in none of these four specimens can any trace of the thyroid gland be found. Microscopically these tumours consist of cysts lined with columnar epithelium, lymphoid tissue, and islands of cartilage. As Keith says, "How the thyroid body of the fœtus comes to assume such a structure and size is an enigma."

CYSTS

[illegible] gether various patho-
logi [illegible] ely in their nature,
agree [illegible] of fluid surrounded
by a wall of connective tissue lined with epithelium or endothelium.

Localized collections of fluid, due to pathological causes, are so common that it is difficult to frame a satisfactory definition which shall distinguish cysts from other collections, and the distinction is largely an arbitrary one. Certain conditions can readily be excluded, such as (1) natural spaces distended with fluid, e g. a hydrocele of the tunica vaginalis, a distended bursa, or a tubo-ovarian cyst; (2) hollow organs distended by excretions or secretions, such as hydronephrosis, or a distended gall-bladder; and (3) cysts present in tumours, (*a*) resulting from various accidental conditions, such as hæmorrhage or degeneration, or (*b*) occurring as an essential feature of the growth, as in cystic adenoma of the breast. A true cyst usually presents itself as a definite localized "tumour," and is often capable of being removed intact from the tissues in which it lies.

According to their mode of origin cysts can most conveniently be classified as follows:—

1. Glandular retention cysts.
2. Exudation cysts.
3. Cysts arising in rudimentary structures or tissue inclusions.
4. Parasitic cysts

1. **Glandular retention cysts.**—Cysts resulting from retention of secretions, often more or less modified, are liable to form in all glands, and are met with in the breast, pancreas, salivary glands, ovary, kidney, and liver. Such special glandular cysts will be considered in connexion with other diseases of the organs in which they occur. Two varieties may, however, be conveniently described here—those arising in the sebaceous glands and mucous glands respectively.

Sebaceous or atheromatous cysts occur in all situations in which sebaceous glands are normally present. They are, however, most common on the scalp and face, are not rare on the neck, shoulders and back, buttocks, scrotum and penis, but are seldom met with on the limbs. They are frequently multiple, and vary in size, but rarely exceed that of a large orange. A sebaceous cyst possesses a fibrous wall lined with one or more layers of flattened epithelium, in which, however, no Malpighian layer or papillæ can be recognized. The contents usually consist of a soft porridge-like material, but occasionally they are thin and milky, whilst in some cysts they form laminated layers almost horny in consistence Examined microscopically, the contents show epithelial débris, fatty granules, and cholesterin crystals.

Although it is certain that sebaceous cysts usually arise from distension of a sebaceous gland, it is probable that some may originate as outgrowths from the hair-follicles.

A sebaceous cyst forms a globular tumour situated immediately beneath the skin The consistence varies with the character of the

contents; it is usually doughy, and may pit on pressure, but it may be elastic or hard. Occasionally the orifice of the duct of the gland from which the cyst originated can be seen in the skin as a small depression or black spot, and at this point the skin is intimately connected with the cyst wall Sometimes the sebaceous material can be squeezed from the orifice of the duct. Over a large cyst the skin often becomes thinned and, in the scalp, bald as the result of atrophy of the hair-follicles The diagnosis of a sebaceous cyst from a chronic abscess or soft lipoma is rarely attended with difficulty, and subcutaneous dermoids can usually be distinguished from sebaceous cysts by their limitation to certain situations, and often by the greater depth at which they lie. Cysts described as "congenital sebaceous cysts" are always dermoids, and the same is almost always true of the cysts in children which are described as sebaceous.

Sebaceous cysts are liable to the following changes: *Inflammation and suppuration* are common, especially in small cysts on the cheek; the contents of the resulting abscess are often very offensive. *Ulceration* of the overlying skin may involve the superficial part of the cyst wall, thus widely opening up the interior. This has been observed chiefly in sebaceous cysts of the scalp, and may lead to a very peculiar appearance resulting from the formation of exuberant masses of granulation tissue from the deep part and edges of the interior of the cyst. The condition may thus closely simulate a malignant growth.

Another change occasionally occurring in a sebaceous cyst is that which results in the formation of a *sebaceous horn* The contents of the cyst gradually escape from an orifice in the cyst wall and skin, and form a slowly increasing conical, horny mass, which may superficially have a close resemblance to the horny epidermic outgrowths that sometimes form on the surface of cutaneous papillomas (p. 479).

Calcification of the cyst wall and its contents may occasionally convert a sebaceous cyst into a solid mass, sometimes wrongly described as bony. This change is most common in small cysts in the region of the shoulder, but may occur in cysts in the scalp or elsewhere. The supervention of *malignant disease* in the form of squamous-cell carcinoma in a sebaceous cyst is very rare.

In removing a sebaceous cyst, care must be taken that the cyst wall is completely taken away. In large sebaceous cysts of the scalp this can most easily be done by evacuating the contents through a short incision, and then carefully drawing out the cyst wall.

Mucous cysts arise as retention cysts of the mucous glands which are present in mucous membranes. They rarely reach a large size, and appear usually as small, tense, semitranslucent bluish prominences, containing a clear viscid fluid. They are not uncommon

on the mucous surface of the lips and cheeks, and are occasionally met with on the tongue.

The name *ranula* is applied to a cyst sometimes found in the floor of the mouth beneath the tongue to one or other side of the middle line. The cyst, which may extend on to the under-surface of the tongue, forms a bluish, semitranslucent prominence, and contains thick, ropy mucus. It is unconnected with the salivary glands, and the patent duct of the submaxillary gland can usually be demonstrated, lying on the surface of the cyst. The exact origin of a ranula is uncertain, but in view of its very constant anatomical relations it may be assumed that its origin is also constant. According to one view, a ranula is a simple mucous retention cyst arising in some special mucous gland, such as the gland of Blandin, which lies on the under-surface of the tongue, or the incisive glands, which lie close to the lower jaw opposite the central incisor teeth. Thompson of Galveston has recently recorded cases in which a cyst in the mouth, having the character of a ranula, was associated with a cyst in the neck, apparently of branchial origin, and suggests that the ranula itself is also of developmental origin and derived from a lower branchial cleft displaced upwards in the process of elongation of the neck.

Mucous cysts are sometimes met with in the labia minora. A specimen of this kind, removed by Liston, is as large as a Tangerine orange. A cyst sometimes of large size may develop from Bartholin's gland, forming a tumour in the posterior extremity of the labium majus. Occasionally a cyst of this kind suppurates.

2. **Exudation cysts** are cysts which arise from an exudation of fluid from the lymphatics or blood-vessels. When such an exudation of fluid, whether it be serous, chylous, or sanguineous in character, occurs into an already existing cavity, such as a joint, bursa, or other serous cavity, the resulting collection is not properly included among cysts; whereas in a true exudation cyst the wall of the cyst, as well as the fluid it contains, is a distinct new formation.

According to the character of the fluid, exudation cysts are divided into serous, chylous, and blood cysts.

True serous cysts are rare, and must not be confused with cystic lymphangiomas (p. 446). As examples may be mentioned certain cysts of the mesentery, which may be large enough to produce an abdominal tumour, and in some instances have occasioned intestinal obstruction.

Serous cysts are often described as one variety of cyst of the breast. Undoubtedly a single thin-walled cyst containing clear fluid sometimes occurs in this situation, but the evidence that it arises independently of the gland tissue does not appear conclusive.

Chylous cysts are occasionally found in the abdominal cavity, and constitute a rare form of mesenteric cyst.

Blood cysts.—These, although rare, deserve brief notice. It occasionally happens that a hæmatoma of the subcutaneous tissues, or in other situations, instead of being gradually absorbed, undergoes changes which result in the formation of a true blood-cyst. This consists of a fibrous wall, the inner surface of which is covered with a thin layer of rusty-coloured material (hæmatoidin), the contents being a clear yellow fluid.

Cysts of this nature (apoplectic cysts) are occasionally found in the cerebral membranes or in the substance of the brain.

The reader may be reminded that many so-called "blood cysts," met with in connexion with the bones and in other situations, prove to be tumours, usually myeloma or sarcoma, in which the tumour substance has been broken down by hæmorrhagic extravasation.

3. **Cysts arising in tissue inclusions or vestigial structures.**—**Dermoid cysts** are the most important examples of this class. They may be defined as cysts of congenital origin lined with skin or mucous membrane, and they may arise either in a rudiment of the surface which has remained included in the deeper tissues or in a vestigial epithelium-lined structure. The most simple dermoids are those which occur in the situation of various embryonic fissures, the edges of which come into contact and eventually unite. During this process it is easy to understand how a rudiment of the surface epiblast may remain embedded in the deeper tissues and become the origin of a dermoid cyst.

Bland-Sutton, to whom we owe much of our knowledge of these tumours, distinguishes by the names *sequestration dermoids* and *tubulo-dermoids* those arising in surface inclusions and in epithelium-lined vestigial structures respectively.

A simple dermoid cyst consists of a fibrous wall lined with stratified squamous epithelium in which the papillary arrangement normal to the skin is often well marked, and in addition various cutaneous appendages, such as sebaceous glands, hair-follicles, and less frequently sweat-glands, may be present (Fig. 168). In dermoid cysts occurring in *teratomas*, which have already been described, other structures such as teeth, nails, and more complex parts may be present.

The contents of a dermoid cyst vary, but most commonly consist of the sebaceous material secreted by the sebaceous glands in its wall, and thus resemble the contents of a sebaceous cyst, often with fine hairs projecting from the wall. If, however, no sebaceous glands are present, the cyst may contain a clear or opalescent fluid and be translucent.

Dermoid cysts of the head and neck.—The most common situation for dermoids is the *face*, the exact position being usually

determined by the lines of union of the various processes from which the part is developed. They thus occur in the fissure between the maxillary process and the frontal region of the cranium with its central fronto-nasal process, and also in the fissure between the maxillary and mandibular processes.

A dermoid arising in the first of these fissures may be situated at the outer angle of the orbit, less commonly at the inner angle, and still less commonly in the naso-facial sulcus, whilst a dermoid arising in the cleft between the maxillary and mandibular processes is situated

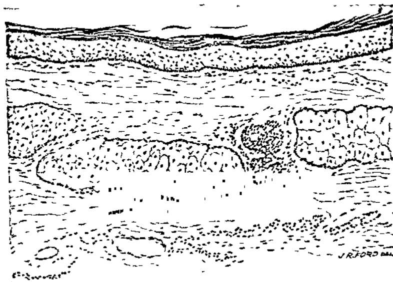


Fig. 168.—Microscopic section of wall of dermoid cyst, showing the stratified epithelial lining and sebaceous glands.

on the cheek in a line drawn from the external auditory meatus to the angle of the mouth.

The cyst which is so frequently found at the outer angle of the orbit is by far the most common example of a sequestration dermoid (Fig. 169). It rarely reaches a large size, and, although it usually lies close to the external angular process, it is sometimes found in the outer end of the upper eyelid. The cyst is usually deeply seated beneath the orbicularis, lying on the bone, in which it may occupy a shallow depression. A dermoid cyst is occasionally situated in the middle line at the *root of the nose*. In two cases of this kind we have confirmed Bland-Sutton's observation that the cyst may be translucent. In one of these cases we found the nasal bones to be separated by the cyst, which extended so deeply that after its removal the upper

edge of the nasal septum was exposed and each nasal cavity opened. The mode of origin of such a cyst is obscure, but a fine process of the dura mater can be demonstrated in the infant between the nasal bone and the cartilaginous capsule of the nose, and possibly a dermoid in this situation may be of intracranial origin.

Dermoids of the *scalp* are most common at the external occipital protuberance and over the anterior fontanelle. When in the latter situation the cyst may be firmly connected with the membrane closing the fontanelle, and when lying over the bone a depression or perforation may be present, and the cyst may even be attached to the dura mater.

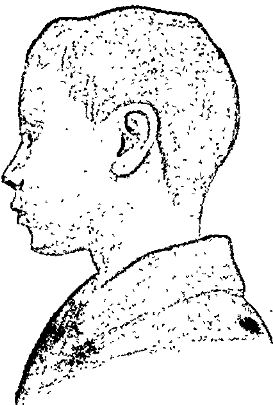


Fig. 169.—Orbital dermoid.

Dermoids of the *external ear* probably arise in the clefts between the seven processes from which, according to His, the part is developed. Such a cyst may present itself as a tumour over the mastoid process, and in a case of this kind dissection showed that the cyst could be easily separated from all the surrounding tissues except in front, where it was intimately connected through the cartilage with the skin lining the hollow of the concha.

Intracranial dermoids are rare. According to Bland-Sutton, they are usually in the occipital region, and nearly always in relation with the tentorium cerebelli. They have also been found in the brain, sometimes in connexion with the ventricles, and may be multiple. Certain cysts in this situation are very rich in cholesterin, and the name "cholesteatoma" has been applied to them; and it is probable that while some such tumours are true dermoids, others are of endothelial origin, and that the peculiar formations are allied to the concentric bodies found in the psammomas (p. 453) It may here be noted that the name cholesteatoma is also applied to the peculiar laminated masses sometimes found in the tympanum and mastoid

antrum, and resulting from a gradual accumulation of epithelial débris and inflammatory exudation.

Dermoid cysts of the *tongue* probably owe their origin to inclusion of epithelium at the line of union of the median and lateral tubercles from which the tongue develops (sequestration dermoids), or arise in an unobliterated segment of the thyro-glossal duct or canal of His (tubulo-dermoids) A lingual dermoid may be situated mesially or laterally, and usually presents itself as a tumour in the floor of the mouth which may also project beneath the jaw. An origin in the thyro-glossal duct is assigned to those cysts which lie deeply in the middle line between the genio-hyo-glossi muscles, in the position occupied by the duct as it passes from the foramen cæcum at the base of the tongue to the deep aspect of the hyoid bone. An extraordinary example of lingual dermoid is preserved in the Museum of University College Hospital. It was removed by Gray of Bombay, and formed an enormous tumour protruding from the mouth, and containing two pints of sebaceous matter.

Dermoid cysts of the *neck* may occur in the middle line or laterally. In the middle line they arise in connexion with the union of the lateral halves, but when situated laterally they originate from one of the branchial clefts A branchial dermoid usually presents itself as a deeply seated cyst situated slightly below and behind the angle of the jaw, and its removal may involve an extensive dissection exposing the bifurcation of the carotid artery. The position of such a cyst suggests that it has its origin in the second branchial cleft, which passes from the tonsillar region between the internal and external carotid arteries In a case of this kind under the care of Godlee, the cyst was mistaken for a softened tuberculous gland, and its nature was only discovered after the cyst had been removed intact.

Dermoids of the trunk may occur at any point along the middle line, but have most commonly been found over the sternum and at the umbilicus. Over the spine they have been mistaken for spina bifida, or may be associated with it. It has already been pointed out that dermoids of the scrotum must be carefully distinguished from dermoid cysts in teratomas of the testicle (p. 622). Bland-Sutton refers to a dermoid cyst containing sebaceous matter and hair, which he removed from the labium, and cysts lined with stratified squamous epithelium are occasionally found in the lower part of the vagina.

Cysts of epidermic structure, and throwing an interesting light on the mode of formation of congenital dermoids, are sometimes met with as the result of injury, usually a punctured wound, and evidently caused by the displacement of a fragment of living skin into the deeper tissues. Such cysts are called *implantation cysts* or *traumatic dermoids.* They rarely reach a large size, and have been found most frequently

on the palmar surface of the fingers, where punctured wounds are common. Similar cysts have been met with in the iris and cornea.

Another striking illustration of dermoid cysts arising by accidental implantation is sometimes seen in the formation of small cysts of this nature which may occur on the peritoneum as the result of rupture of an ovarian dermoid.

Many instances of **cysts arising from vestigial structures** occur in different organs, and only need mention here. Thus, the *parovarian cyst in the broad ligament undoubtedly arises in the remains of the Wolffian body and duct; certain vaginal cysts are supposed to arise from the duct of Gartner or from diverticula of the Müllerian duct; cystic disease of the kidneys and liver is believed to be due to dilatation of rudimentary tubules in the organs; while certain cysts of the testicle (encysted hydrocele of the epididymis) are supposed to arise in vestigial structures representing remains of the Müllerian duct or vasa aberrantia.

4. **Parasitic cysts.**—The only form of parasitic cyst that is common in the human subject is that which occurs as the hydatid form of the *Tænia echinococcus*, the tapeworm of the dog, and is known as the **hydatid cyst.**

It is a characteristic of the tapeworms, or cestodea, that the two stages of their development are passed in two separate hosts. Thus in the case of *Tænia solium* the adult worm forms the most common tapeworm in the human subject, while the hydatid stage occurs as the cysticercus or "measle" of the pig, although occasionally the cysticercus is met with in man. The life-history of the *Tænia echinococcus* and its hydatid form is as follows: The adult worm is found in the intestine, especially the duodenum, of the dog or wolf, and appears to the naked eye as a small white spot on the mucous membrane. It consists of four segments and measures 4 mm. in length; the head is provided with four suckers and thirty or forty booklets (Fig. 170). The ripe terminal segment or proglottis, containing several hundred ova, becomes detached and is passed in the excreta, the ova being set free by the rupture of the proglottis. An ovum now reaches the alimentary canal of man, probably, as a rule, in contaminated drinking-water, and after digestion of the envelope in the stomach the six-hooked embryo is set free. This has the power of actively making its way through the stomach wall, and, as it is scarcely larger than a red blood-corpuscle, is readily carried to the liver or lungs or to some other part. Having become arrested, the embryo develops into a cyst, in which further stages of development occur. The wall of the parasitic or hydatid cyst consists of an outer elastic laminated cuticular layer and an inner granular or parenchymatous layer, whilst around

the true cyst a pseudocyst develops as the result of inflammatory reaction in the surrounding tissues of the host. The fluid contained in the cyst is colourless and clear, or slightly opalescent, reaction neutral, specific gravity 1002 to 1005; it is non-albuminous, and contains some chloride of sodium with sometimes a trace of a reducing agent. By the time the cyst has reached the size of a walnut a number of "brood capsules" begin to form on the inner surface, and appear

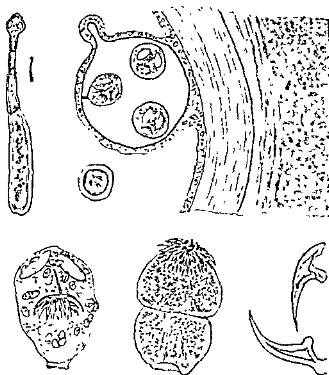


Fig. 170.—Diagram showing Tænia echinococcus (natural size and enlarged), an ovum, section of wall of hydatid cyst with brood capsule and scoleces, two scoleces and hooklets.

as small bodies like pins' heads Each brood capsule also consists of two layers, but the cuticular layer is internal, and on it a number of heads or scoleces (Fig. 170) form, which fail to undergo further development unless they reach the alimentary canal of a suitable host, such as the dog, when they become the heads of a new generation of adult worms The hydatid form of *Tænia echinococcus* is met with in several of the lower animals, such as the sheep, cow, and pig, as well as in man, and it is from the offal of such animals that the *dog becomes infected*. The hydatid cyst, as it occurs in man, may be single or multiple, and varies in size within wide limits, some of

the largest containing many pints of fluid. In addition to the development of brood capsules and scoleces as above described, a very common occurrence is the formation of secondary or "daughter cysts" in or outside the parent cyst. When the daughter cysts arise *internally* they are formed from the brood capsules or scoleces, and may themselves proceed to develop in a similar way; they often escape in the form of grape-like cysts when the parent cyst is opened. Such a cyst is called *endogenous*. When the daughter cysts arise *externally* they originate between the laminæ of the cuticular layer of the parent cyst and project into the surrounding tissues. Such a cyst is called *exogenous*.

A rare variety of hydatid cyst, which has been found in the liver, consists of a mass of small cysts giving to the whole an alveolar structure. This variety was originally mistaken for colloid cancer until its true nature was discovered by Virchow, who gave it the name *multilocular hydatid*. In the tissue around the cysts large numbers of giant cells may be found. It occasionally happens that the parent cyst or some of the daughter cysts may fail to produce brood capsules and scoleces. Such a sterile cyst is called an *acephalocyst*.

Secondary changes.—The length of time during which a hydatid cyst may remain alive is not known, but certainly it may live for many years. If the parasite dies the cyst ceases to enlarge, and subsequently shrinks; the fluid disappears, and a convoluted gelatinous mass remains, the wall of which may be extensively calcified. Rupture of a hydatid cyst may occur into one of the hollow viscera, the heart or large blood-vessels, a serous cavity, or externally. Suppuration is not uncommon, and the true origin of the abscess may only be determined by the detection of hooklets or fragments of the ectocyst in the pus.

The **geographical distribution** of hydatid disease is largely dependent upon the extent to which infested dogs come into relation with the inhabitants; thus, whilst it is uncommon in Europe and very rare in America, it is common in Australia, Iceland, and other parts.

A study of the **anatomical distribution** of the disease shows that the liver is affected in more than one-half of the cases; thus, among 420 cases treated consecutively in the Royal Prince Alfred Hospital in Sydney, McLaurin found that the liver was affected in 267, or 63.4 per cent. Among the other parts which may be affected are the alimentary canal, lungs and pleuræ, kidneys, female genital organs, brain, muscles, bone, and the heart and blood-vessels.

The **clinical features** of a hydatid cyst necessarily differ widely according to its situation. Thus, in the liver the cyst may form a prominence in the epigastric region, and may project upwards so as to displace the heart and produce physical signs resembling those of pleural effusion. When a hydatid cyst is sufficiently superficial,

distinct fluctuation may be felt in it, and sometimes a peculiar vibratory sensation—the so-called hydatid fremitus—is felt when the tumour is palpated with the fingers of one hand whilst another part of the tumour is sharply tapped with the fingers of the other hand. In other regions of the abdomen a hydatid cyst may simulate many other conditions, such as a hydronephrosis or a cyst of the ovary.



Fig. 171.—Hydatid cyst of orbit.

In the consideration of an obscure case in which multiple abdominal tumours are present, the possibility that they may be hydatid cysts should always be remembered

In the lung the symptoms and physical signs of this disease vary greatly. Hæmoptysis and cough are common, whilst displacement of the heart and the presence of " a rounded area of dullness on percussion, the note obtained being absolutely dull in the centre of the area and gradually increasing in resonance towards its margin, the breath sounds and vocal resonance over the same site being absent " (Fowler and Godlee), are valuable signs Hydatid cysts causing tumours in peripheral parts such as the bones and muscles are very apt to be

mistaken for other diseases, especially in countries in which hydatid disease is rare. In the case of Bilton Pollard's illustrated in Fig. 171, the proptosis caused by a hydatid cyst of the orbit was thought before operation to be due to an orbital sarcoma.

The rupture of a hydatid cyst may in certain situations prove immediately fatal, as, for instance, when it occurs into a large bronchus or blood-vessel. In other cases the detection of hooklets or fragments of membrane in the sputum, vomit, stools, or urine has revealed the nature of an otherwise obscure condition. When a hydatid cyst leaks or ruptures into the peritoneal cavity the results vary considerably in different cases. Sometimes peritonitis with effusion rapidly occurs, but occasionally, as McLaurin has pointed out, a thin adventitious membrane forms around the fluid if the latter only escapes gradually, and a condition much like tuberculous peritonitis may result. Further, it is of interest that the peritoneal reaction may take the form of small multiple granulomas like miliary tubercles.

A phenomenon sometimes accompanying leakage from or aspiration of a hydatid cyst is the so-called hydatid rash. The rash is usually urticarial in character, but it may resemble that of scarlet fever or of measles; it is due to the absorption of some toxic constituent of the fluid.

Another interesting observation which has often been made in cases of hydatid disease is the increase of the eosinophile cells of the blood. Barling and Welsh of Sydney, who have made observations on this phenomenon, found that in 50 per cent. the eosinophilia was marked, in 25 per cent. moderate, and in 25 per cent. absent or so slight as to be of no diagnostic value. It was a salient feature in six cases in which the cyst had leaked or ruptured into the abdominal cavity.

Use has been made of a complement-fixation reaction in the diagnosis of hydatid disease. Fairley of Melbourne, who has investigated the subject, regards the method as of great practical utility, and has found that in a series of 83 cases, 70 gave a positive result, whereas the reaction was negative in 917 cases in which there was no evidence of hydatid disease.

The **treatment** of a hydatid cyst should, as far as possible, consist in the complete removal of the parasitic cyst. Exploratory puncture with an aspirator needle is a dangerous procedure in hydatids of the chest and abdomen, and an exploratory incision should always be preferred. In some situations it may be possible to close the wound after the removal of the cyst, but, especially in large hepatic cysts, the edges of the incision in the adventitious cyst should be sutured to the edges of the wound in the parietes and the cavity drained. Some surgeons think it advisable to inject a small quantity of formalin into the cyst before opening it. In hydatid disease of bone it may be

possible merely to remove the cyst, but, as the disease often assumes the exogenous form in the cancellous tissue, removal of part of the bone, or even amputation, may be necessary.

Hydatid disease in such a situation as the liver must be regarded as a very serious affection, as far as ultimate cure is concerned. McLaurin is of opinion that the subjects of the disease should not be accepted for life assurance for five years after operation.

The only other parasitic cyst of the human subject which needs mention is the *Cysticercus cellulosæ*—the hydatid form of the *Tænia solium*. Usually this hydatid occurs as the "measle" of the pig, and its occurrence in man is rare

The cysticercus consists of a thin-walled cyst varying in size from a pea to a small bean, and presenting on its inner surface a small projection or scolex which is capable of developing into a mature *Tænia solium* if conveyed into the intestine of a suitable host.

Among the situations in which cysticerci have been found in man are the brain, eye, muscles, subcutaneous tissues, heart, and viscera. They may be accidentally discovered post mortem, but have been known to occasion symptoms during life, as, for instance, when situated in the brain. A cysticercus in the vitreous body of the eye may form a striking object on ophthalmoscopic examination.

Multiple subcutaneous cysticerci may resemble small solid tumours and their nature be detected only after excision. In a case of this kind under the care of Rose Bradford, the patient, a soldier aged 30, was admitted to hospital on account of epileptic attacks. Multiple small tumours, one of which was excised and proved to be a cysticercus, were present in the subcutaneous tissues of the scalp, trunk, and limbs, and beneath the tongue. The epileptic attacks were probably due to a cysticercus of the brain.

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EXAMINATION OF THE BLOOD AND OF THE CEREBRO-SPINAL FLUID

BY J. M. BEATTIE, M.A., M.D.

EXAMINATION OF THE BLOOD

THE surgeon cannot afford to dispense with blood examination as an aid to diagnosis For differential diagnosis, of course, he needs it. For example, a case of tuberculosis may be closely simulated by a case of typhoid fever; a case of pyæmia may present the paroxysmal fever of malaria Blood examination in such cases would not only be an aid to, but might definitely settle, the diagnosis. Therefore, without wishing to magnify the importance of blood examination, I hold that more accurate diagnoses might be made if it were more largely practised; and if it were a routine practice with both surgeon and physician much valuable information would be obtained and there would be, at any rate, less dogmatism from the cytologist and less contempt for his observations from the surgeon.

It is unnecessary here to deal with the blood pictures of pernicious anæmia, of the various forms of leukæmia, and of those other diseases which do not call for surgical interference, and in which the examination of the blood is the determining factor in the diagnosis.

CHEMICAL AND PHYSICAL CHARACTERS OF THE BLOOD

Glucose in very small quantity is usually present, and has been found to be increased in pancreatic diseases, especially in diabetes mellitus.

Glycogen is referred to later under Iodophilia (p 644). The value of its presence as a factor in diagnosis by blood examination is very doubtful. It is, however, found, sometimes in large amount, in the leucocytes in acute inflammatory and suppurative diseases, in septicæmia, and in diabetic gangrene.

Bile-acids and **bile-pigments** are present in conditions giving rise to jaundice.

Coagulability.—The investigation of the coagulability of the blood is of importance in connexion with "bleeders." In such cases it may be indefinitely delayed; but delay also takes place in the acute infective fevers, in some of the anæmias, and in cases of jaundice; and some surgeons will not operate in cases of jaundice in which the coagulation-time is delayed. The coagulability may be increased, e.g. in pneumococcal infections, and intracardiac or vascular thrombosis becomes an important complication.

The **freezing-point of the blood** has been investigated, especially in diseases of the kidney, the freezing-point being lowered by the presence of greater quantities of dissolved salts, etc.

Blood types.—Though the value of transfusion of blood has been generally recognized in the treatment of cases of hæmorrhage, etc., the occurrence of serious symptoms, such as vomiting, dyspnœa, convulsions, etc., and even death, in certain cases, made surgeons hesitate to use this method of treatment. It is now established that these symptoms were due to the intravenous injection of an "incompatible" blood. Four definite types of blood have been recognized, and before transfusion takes place the suitability of the donor must be ascertained. The patient's blood must not agglutinate nor hæmolyse the red blood-corpuscles of the donor. Having obtained a suitable donor, the risks of transfusion are greatly minimized, if not entirely eliminated. Moss's table of suitability is given in the section on Blood Transfusion (p. 333), where also is described the technique for determining the reaction.

MICROSCOPICAL EXAMINATION

For the surgeon, blood examination is almost synonymous with leucocyte-counting, for it is on the increase of the leucocytes that the surgeon may have to depend both for aid in his diagnosis and for help in determining the time for operation. (Plate 35, Fig. 1, and Plate 36, Figs 1, 2.)

Leucocytosis.—Strictly speaking, this term means an increase in the white cells of the blood, but it has come to be used especially for those cases in which there is an absolute increase in the **polymorphonuclear cells** in the peripheral blood (Plate 35, Fig. 1). This increase may be physiological or pathological.

Physiological increase is seen *after food*, but this increase is never very considerable. Attempts have been made to utilize this digestion-leucocytosis as an aid to differential diagnosis between simple ulcer and cancer of the stomach, it being alleged that in the latter digestion-leucocytosis is absent. This statement, however, is not fully borne out, for in some cases of gastric cancer the leucocytosis certainly occurs.

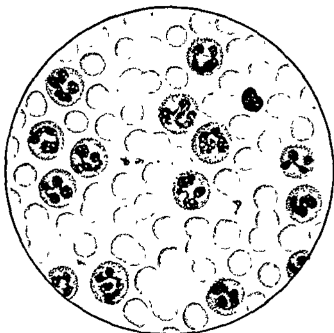


Fig 1 —Polymorphonuclear leucocytosis

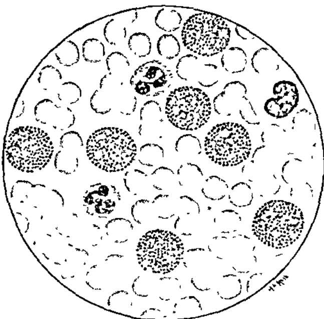


Fig 2 —Eosinophilia

PLATE 35

During the last months of *pregnancy* the leucocytes may reach an average of 12,000 or 13,000. By some authorities—e.g. von Limbeck—this is regarded merely as a digestion-leucocytosis, brought about by the need of additional nourishment for both mother and child. Others regard the leucocytosis as a result of auto-intoxication.

Apart from the conditions stated, it may be taken as a general rule that a leucocytosis of 12,000 or more means the absorption of toxic or bacterial products, and must be regarded as a means of protection A good leucocyte response is favourable, and a feeble leucocytosis means very often that the attacking agent is extremely virulent, or that the leucocyte-forming tissues are exhausted. The severity of an attack is not proportioned to the leucocytosis; a very slight abscess may bring about a great increase in leucocytes, whilst a fatal infection may give rise to a very slight increase. On the other hand, a good leucocyte response very often means a hopeful prognosis.

A leucocytosis, no matter how marked, is of no value in determining the site or even the exact nature of the focus of infection. Thus, acute cerebro-spinal meningitis will give a leucocyte count of 40,000, but a similar degree of leucocytosis may be found in a case of peritonitis. Localized pus-formation in any part of the body gives rise to a leucocytosis, and it is therefore obvious that blood examination can only be of value in combination with other diagnostic methods.

A single examination of the blood may in some cases be of great value, but systematic and regular examination from day to day is much more important, at any rate from the point of view of the surgeon.

It may be laid down as a general rule that, in a man whose leucocyte-forming tissues are in good condition, a gradually increasing leucocytosis means a gradual spread of the inflammatory process, and therefore may be an indication for operative interference.

Emerson states that at the Johns Hopkins Hospital, in appendicitis and in all acute abdominal cases, after the first suggestive symptom the leucocytes are counted every hour, and that with a rising leucocytosis an operation is performed without delay, even though the abdominal signs are very slight. If the leucocyte number is high but stationary when the patient is first seen, one can wait; but if rising even slightly, there should be no delay.

It should always be remembered that a normal count is of little importance, some of the most severe and fatal cases showing no increase in leucocytes. A count of 12,000 to 15,000 indicates an active inflammatory process, and one of 20,000 or more probably means definite abscess-formation with absorption of toxic products.

Typhoid fever.—A count at regular and short intervals is of great importance, especially in a case where the possibility of perforation is being considered. Normally the leucocytes are not increased in this disease, and an increase always means the onset of some complication. The exact nature of the complication cannot be determined from the leucocyte count alone, but the knowledge of this blood alteration puts the surgeon on his guard. If the abdominal symptoms indicate perforation, the surgeon will operate, irrespectively of any leucocyte count; but with a rising leucocyte count and with very slight local signs an operation would also be justifiable. Emerson claims that in the Johns Hopkins Hospital 30 per cent. of the cases of perforation have been saved by proceeding to operation on the evidence of a rising leucocyte count, always, of course, in combination with other diagnostic methods.

Malignant disease.—In about 60 per cent. of cases there is a moderate leucocytosis, which seems, however, to depend partly on the site of the tumour, the effect it has upon the nutrition of the patient, and the amount of hæmorrhage and necrosis that is present. Little value, however, can be given to leucocytosis as a diagnostic aid. It bears no relation to the kind of tumour, though it is more common with sarcomas than with cancers, and it bears little upon the situation of a tumour. In malignant stricture of the œsophagus there is generally a leucopenia, but this is the leucopenia of starvation; in cancer of the stomach a leucopenia is of frequent occurrence, though a leucocytosis is more common. It is said that the leucocytosis is generally high in cancers of the thyroid, pancreas, and kidney.

In **intestinal obstruction,** according to Emerson, the leucocytes rise rapidly to about 16,000 when partial, to 20,000 or more when complete; with over 20,000 cells within the first twenty-four hours, the chances are in favour of gangrene

Tuberculosis and **syphilis** show the same variation in regard to leucocytosis in different cases, and, in consequence, too much importance must not be attributed to this feature in diagnosis. In uncomplicated cases of *tuberculosis* no leucocytosis may be present, whereas in others a lymphocytosis may be quite marked. In some cases of pure tuberculous meningitis, in its early stage, a polymorphonuclear leucocytosis is found. In certain cases of pulmonary tuberculosis with cavity formation an eosinophilia has been described, and has been regarded as a sign of auto-intoxication from the cavity, since it also occurs after the injection of tuberculin. Acute miliary tuberculosis may present a lymphocytosis or a polymorphonuclear leucocytosis. *Tuberculosis of the serous membranes* perhaps more commonly than not shows no leucocytosis. Emerson reports 22 cases of tuberculous peritonitis with a leucocytosis in only 9; Cabot, 60 cases

with a leucocytosis in 14. In tuberculosis of glands there may be a leucopenia, the leucocytes may be normal in number, or—and especially after caseation has begun—there may be a lymphocytosis. In tuberculosis of bones there is no leucocytosis until a secondary infection sets in.

In *syphilis* a lymphocytosis is seen, especially in the secondary and tertiary stages of the disease; but many cases show no evidence of leucocytosis.

Postoperative leucocytosis.—An increase of leucocytes to even 10,000 during the first twenty-four or thirty-six hours after an operation may be regarded as a normal process, due partly to the necessary absorption of destroyed tissue. The leucocytosis in such cases bears no relation to the pulse and temperature. If, however, the leucocytosis is prolonged beyond thirty-six hours, and especially if it shows a progressive rise, it should lead to the suspicion that septic absorption is taking place.

Posthæmorrhagic leucocytosis.—After a large hæmorrhage there is a rise of leucocytes within about an hour to from 12,000 to 18,000. The leucocytes are principally of the polymorphonuclear type. The increase lasts for only a few days, and therefore is not likely to be mistaken for a leucocytosis due to infection.

Medicinal leucocytosis.—It should always be remembered that the administration of certain drugs, such as the salicylates, as well as certain animal extracts—for example, of the thyroid gland and bone-marrow—may lead to the production of leucocytosis.

Lymphocytosis.—From the surgical point of view, lymphocytosis is of much less importance than polymorphonuclear leucocytosis, and is of very little value in relation to either diagnosis or treatment. It is said to occur in connexion with cervical adenitis in children; but in the majority of cases, at any rate, this is merely the lymphocytosis of tuberculosis In lymphomas, and especially in those of the malignant type, a lymphocytosis may be a salient feature. In syphilitic and in tuberculous infections a lymphocytosis is usually present, though the absolute increase of lymphocytes may not be very great.

Eosinophilia (Plate 35, Fig. 2) is not of special importance to the surgeon. It has been met with in cases of chronically enlarged spleen, and in this connexion it has been suggested that these spleens are functionless, a very considerable eosinophilia having been described as occurring in cases about a year after splenectomy. A large number of skin diseases are accompanied by an eosinophilia, and it is a common manifestation of parasitic infection. In trichinosis and in ankylostomiasis it is of very considerable diagnostic value.

Iodophilia.—In this condition the leucocytes contain definite granules which take on a brownish-red colour when the specimen is treated with iodine This reaction is present in many cases of septicæmia, and, it is said, particularly in those with purulent exudates. Bond states that this iodophilic reaction is found principally in the leucocytes *after* they have emigrated from the vessels, and he has shown that this iodophil substance is constantly found in certain cancer cells of epithelial origin He suggests that there is an association between activity in the production of this substance (glycogen) and resistance to infection.

BACTERIOLOGICAL EXAMINATION OF THE BLOOD

If microscopical examination of the blood is not sufficiently attended to, it may be said that the bacteriological examination is almost entirely neglected by many surgeons, and yet in many cases its value can hardly be over-estimated. The withdrawal of the blood should be treated as a surgical operation, and thorough cleanliness of the skin, the syringe, etc., is necessarily of supreme importance From 10 to 20 c.c. of blood should be withdrawn from the vein chosen, which is usually the median basilic or cephalic. In very obese people it may be necessary to incise the skin; but this should, if possible, be avoided. Where the vein is not prominent, pressure on it above the point of puncture may make it sufficiently evident In young children it is often a great advantage to bandage the arm from the fingers upwards after the upper bandage has been applied.

The blood, immediately it is withdrawn, should be distributed in tubes or flasks of broth, though sometimes a medium specially suited to the organism whose presence is suspected should be used. The amount of blood in each tube or flask varies, in relation to the quantity of medium, from equal parts to 1 in 5 or 1 in 100. As a general rule, the more feebly growing organisms require a greater quantity of blood, but too much blood may inhibit the growth of organisms. After an incubation period of twenty-four hours, examination of the cultures may be undertaken in various ways, the methods differing, of course, for different organisms (*see* under Surgical Bacteriology, pp. 36–108).

The value of blood-cultures.—In cases of general infection with pyogenetic organisms, in osteo-myelitis, etc., the streptococci or the staphylococci may usually be obtained in pure culture. Typhoid bacilli have been demonstrated in the blood in a considerable proportion of cases before even the Widal test has been positive. Pneumococcal infections may show the presence of the organism in the blood.

This information is important for diagnostic purposes, and the above method of procedure is often the easiest and most certain way of getting a culture for the preparation of a vaccine.

Agglutination phenomena.—The Durham-Grunbaum, or, as it is more commonly called, the Widal, reaction for typhoid fever has already been described (p. 47). Its importance in the diagnosis of typhoid fever is unquestioned. This same reaction, however, has a much wider application, and has now been applied to various organisms with more or less definite results. Considerable aid from the reaction is given in the diagnosis of dysentery, paratyphoid and paracolon infections, Malta fever, etc.

Wassermann reaction.—For this test at least 1 c.c. of blood should be withdrawn (*see* p 53).

EXAMINATION OF THE CEREBRO-SPINAL FLUID

Although the examination of the cerebro-spinal fluid as a valuable means of diagnosis is now sufficiently established, it must, like all laboratory methods, be used only to supplement and not to supplant the ordinary clinical investigation of the patient. Thus, the presence of a great excess of lymphocytes in cerebro-spinal fluid does not of itself help us very far in our diagnosis, but in conjunction with the clinical history and clinical examination it may definitely confirm an otherwise doubtful diagnosis of tuberculous meningitis.

The cerebro-spinal fluid is contained in the two great cavities—the ventricles and the subarachnoid space. There seems little doubt that a considerable amount, at any rate, of the fluid is produced within the cavity of the ventricles as a secretion from the choroid plexuses. There is definite communication between the fluid in the ventricles and that in the subarachnoid space by way of the foramina in the roof of the fourth ventricle, but it seems improbable that the whole of the fluid in the subarachnoid space is derived from the choroid plexuses

Free communication exists between the subarachnoid space and the adventitial (perivascular) space of the cerebral and spinal vessels, and Mott has suggested that the fluid gains access directly through fine lymph-channels to the space surrounding nerve-cells. There is distinct evidence, however, that foreign proteins—e.g. tetanus toxin—cannot pass from the subarachnoid space to the nerve-cells.

As the total quantity of the fluid in man is about 60 to 80 c.c., and as secretion is constantly taking place, there must be also a regular absorption of the fluid, the major portion of it passing into the blood. It is calculated that the fluid is renewed completely six or seven times a day.

There is no doubt that the fluid plays an important part in the mechanics of the cranial cavity. It shields the nervous tissue from injury by the blows and shocks it naturally receives, and it is an important mechanism for compensating changes in the cerebral volume. With a rigid cranial wall, the brain can expand only by driving fluid from the cranial into the spinal cavity, and there is abundant evidence that a constant ebb and flow is taking place.

In addition, however, there seems little doubt that the fluid has an important function in protecting the nervous system from the action of harmful substances circulating in the blood. It has been shown that substances such as barium chloride and salvarsan, when injected into the spinal fluid, may produce serious toxic symptoms, whereas they may be given in large quantities intravenously without producing any toxic effect on the brain. Bacterial and other toxins are in a similar manner prevented from reaching the nervous tissue.

Again, the fluid is concerned with the nutrition of, and the elimination of waste products from, the nervous tissue. This is shown by the high carbon-dioxide content, and by the variation in composition at different times.

Lumbar puncture.—This is a very simple operation, and one attended with practically no risk of damaging the spinal cord, as the point of puncture is below the actual limit of the cord and the fibres of the cauda equina are sufficiently movable to escape the needle. It is well to keep the patient in bed for at least twenty-four hours following the puncture, so that the pressure in the cerebro-spinal cavity may become equalized. The patient is placed on the left side near the edge of the bed, the knees flexed upon the abdomen, and the site of puncture prepared as for any surgical operation. The needle used should be fairly strong and from 5–10 cm. long. The site of puncture should be at the lower border of the third lumbar vertebra, and usually slightly to one side of the middle line, or just immediately above a line joining the highest points of the two iliac crests. The needle is directed slightly upwards and inwards until the dural sac is reached, when the cerebro-spinal fluid should flow freely and, if under pressure, with considerable force No aspiration should be used at any time. The needle must be pushed in with sufficient force to penetrate the muscles, etc., and it is therefore most important that care should be exercised lest the needle suddenly strike the vertebra and break.

Normally the fluid resembles distilled [illegible] in appearance, though there may be a slight cloudiness or even [illegible] owish colour. Its pressure varies norm[illegible] 60 to 120 [illegible] er when measured with the patient [illegible] pc [illegible] pathological conditions the pressu[illegible] d [illegible]

No changes of diagnostic importance have been observed either in the reaction or in the specific gravity of the fluid in pathological conditions. The reaction is normally alkaline and the specific gravity 1006–1010. In its normal condition, a very few lymphocytes may be present, and the fluid contains a small quantity of protein, of which the most important constituent is globulin, and about 0·1 per cent. of glucose. In pathological conditions, the albumin-content may be much increased and the sugar may show considerable variation in amount, being absent, according to some observers, in tuberculous and in epidemic cerebro-spinal meningitis. Urea is present in normal conditions, and there are also small amounts of the chlorides of sodium and potassium. Cholin is present normally in very small amount, but in pathological conditions, especially those associated with *nerve degeneration, it may be greatly increased.* The method of determining the presence of these chemical constituents must be left to special books on the nervous system or text-books of diagnostic methods.

PATHOLOGICAL ALTERATIONS

(*a*) **Naked-eye appearances.**—The fluid from a perfectly healthy man is clear and colourless, and this appearance may persist in spite of a considerable increase in the lymphocytes and the albumin content. More commonly, however, in cases in which the increase in lymphocytes is considerable there is a very slight turbidity or opalescence. Where the cellular increase is greater, and especially when the cells are of the polymorphonuclear type, the fluid becomes distinctly turbid and may be purulent. A clear watery but pathological fluid frequently shows, on standing, a fine web of coagulum. This is common in tuberculous meningitis, and has been described in posterior basic meningitis, in poliomyelitis, and in syphilitic meningitis.

Blood admixture is common, and may be due to damage to a vessel at the time of puncture, or to some pathological condition such as intraventricular or subarachnoid hæmorrhage, injury to the spinal column, or intense inflammatory involvement of the membranes.

Bile-staining may be present, but is hardly ever so intense as the bile-staining of the lymph, urine, etc., and this is probably due to the fact that the healthy choroid plexus acts as a barrier to the passage of the constituents of the bile.

(*b*) **Microscopical examination.**—In normal cerebro-spinal fluid the cells are very scanty, a few lymphocytes (not more than 5 per c.mm.) and occasionally an endothelial cell being found. An increase of lymphocytes or the presence of abnormal cells, even in small numbers, is often of great diagnostic importance. Thus,

a few large mononuclear cells are frequently found, according to Buzzard and Greenfield, in cases of tumour invading the walls of the ventricles or involving the meninges, and a few polymorphonuclear and phagocytic cells may be present when a brain abscess lies in close relation to the meninges. An increase of lymphocytes from 20 to 100 or even 200 to 500 per c.mm. is found in syphilitic meningitis, in general paralysis, and in tabes. This lymphocytic increase is very considerable in tuberculous meningitis, but it is not uncommon to find a large number of polymorphonuclear cells, in addition, in this disease. In acute meningitis due to pyogenetic organisms the cellular increase is very great, but the majority of the cells are of the polymorphonuclear variety.

In *poliomyelitis and polioencephalitis the increase is mainly* in the mononuclear, but there is usually also a small proportion of *polymorphonuclear cells.*

(c) **Chemical examination.**—The fluid should always be tested for the total albumin and for the serum-globulin. In *syphilitic disease* of the nervous system the *serum-globulin* is considerably increased, in some cases approaching in amount the total albumin content. The increase of serum-globulin is present in other than syphilitic diseases, but its proportion to the serum-albumin is always less than in syphilitic diseases. Buzzard and Greenfield state that "if a positive globulin reaction is obtained from a fluid with a total albumin content of less than 0·04 per cent, there is a strong presumption that the case is syphilitic."

An increase of *albumin* occurs in tuberculous and in meningococcal meningitis, and in cerebral œdema, e g in uræmia. According to Mott, the fluid is especially rich in *nuclein* in progressive paralysis, and lipoids are increased in the fluid in degenerations of the central nervous system.

Glucose is increased in diabetes mellitus, and it is also above the normal amount in all acute infective diseases associated with a polymorphonuclear leucocytosis. The percentage, however, is decreased in all cases of meningeal inflammation.

The *chlorides* are normally very constant in amount (0 70 to 0 76 per cent.), and abnormal percentages are always of importance. An increased percentage indicates renal inadequacy. Low percentages are evidence of serious meningeal infection. According to Mestrezat a percentage below 0 6 is found only in tuberculous meningitis, and he regards the evidence as so important that he places it second only to the finding of the tubercle bacillus in the diagnosis of this disease.

(d) **Loculation syndrome (syndrome of Froin).**—In certain pathological conditions there is a very great increase in the protein content of the cerebro-spinal fluid, which also acquires

a yellowish tint. Fibrinogen is usually present, and may be so abundant that the fluid coagulates almost immediately after withdrawal. These appearances were described by Froin in 1903. Other changes may be present, but the most important of these is the presence, in some cases, of albumoses and peptones due to the autolysis of the albumins. Such fluids are found in cases of spinal tumour and in Pott's disease, and sometimes in cases of chronic meningitis. The view generally taken of these cases is that the cerebro-spinal fluid is localized by some pathological condition and shut off completely, or almost completely, from access to the lower part of the spinal theca. It has been stated definitely that cerebro-spinal fluid containing over 1 per cent. of albumin is shut off from communication with the ventricular system.

The cell content in these cases varies. It may be *high*, as in syphilitic meningitis, or *low*, as in spinal tumour, Pott's disease, chronic basal meningitis, acute myelitis, or extradural tumour or abscess.

(*e*) **Wassermann reaction.**—The examination of the cerebrospinal fluid for the Wassermann reaction is equally, if not more important than the examination of the blood. It may be positive when the blood is negative—a very frequent occurrence in cases of tabes

A positive Wassermann reaction in the blood and cerebro-spinal fluid, a lymphocytosis, and a positive globulin reaction in the cerebrospinal fluid are definitely diagnostic of syphilitic disease of the nervous system, but it is unsafe to base a positive diagnosis on any one of these four reactions.

(*f*) **Lange's colloidal gold reaction.** — Some observers claim that the results obtained with this test are too uncertain to be of great diagnostic value—the so-called "syphilitic curve," they say, may be given by a variety of conditions which are not syphilitic. The test is a very delicate one, and many of the contradictory results are certainly due to faulty reagents and technique Adams and Scott regard the test as of extreme value in the diagnosis of early nervous disease, and have shown that declared luetic and paretic reactions may be obtained although the cell count and protein content are normal and the Wassermann reaction is negative.

CHANGES IN SPECIAL DISEASES

Tuberculous meningitis.—The fluid may be clear, opalescent, or even distinctly purulent. The cellular constituents are in most cases mononucleated cells—lymphocytes or cells of the lymphocyte type (Plate 37, Fig. 1.) In some cases, however, especially in children, the main mass of the cells may be of polymorphonuclear

type, and a positive diagnosis can only be given if the *Bacillus tuberculosis* is found in the films, or if, as the result of inoculation, tuberculosis is produced. No doubt a lymphocytosis (if the clinical symptoms point to meningitis) always suggests tuberculosis; but many errors have undoubtedly arisen from too much dependence *being placed on this single piece of evidence. It has been shown conclusively that a lymphocytosis occurs in cases of general paralysis* and in *locomotor ataxy*. These cases do not usually give rise to any confusion, but this lymphocytosis is also present in syphilitic lesions of the cord and membranes, in chronic posterior basic meningitis (cerebro-spinal meningitis), in any chronic irritative process, and in the later stages of the more acute infections; whereas, on the other hand, a polymorphonuclear leucocytosis, as has been already pointed out, may be a marked feature in some cases of tuberculous meningitis. It is claimed that the lymphocytosis occurs to a greater degree in tuberculous cases than in other pathological conditions; but, even if this is the case, only accurate counting and comparison with a large number of cases can be of any value in forming a differential diagnosis, and this is usually quite impracticable. With our very best counting methods the limits of error are considerable, and with the methods in common use reliable information is impossible. Some workers have especially distinguished between the lymphocytes and the plasma cells, and claim that the cells found *in general paralysis and in cerebral syphilis are of this type* and not the ordinary lymphocytes

Reference has already been made to the increase in albumin and the decrease in chlorides in this condition.

Epidemic cerebro-spinal meningitis.—The fluid may be transparent, opalescent, or purulent, but the cellular elements are, in the vast majority of cases, of the polymorphonuclear type (Plate 37, Fig. 2). The characteristic organism (meningococcus of Weichselbaum) (*see* p. 69) is found in the cells, and on its presence the diagnosis is based.

Not uncommonly this organism may be associated with other bacteria, such as the pneumococcus, streptococcus, etc.

Purulent meningitis.—A purulent exudate may be found, as has been stated, in tuberculous or in epidemic cerebro-spinal meningitis. More commonly, however, the purulent cases are due to other organisms—e g. the pneumococcus, streptococcus, *B. influenzæ*, etc. During the early stages the exudate is composed mainly of polymorphonuclear cells, but in the later stages, and especially during convalescence, cells of the lymphocyte type may be present in considerable numbers. Diagnosis of the causal organism can *only* be made by careful bacteriological examination.

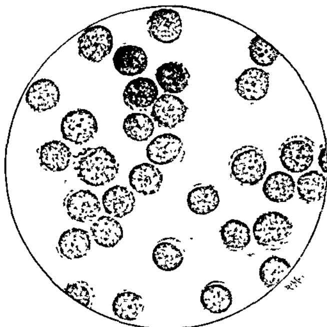


Fig. 1.—Cerebro-spinal fluid, got by lumbar puncture, showing lymphocytosis. (From a case of tuberculous meningitis.)

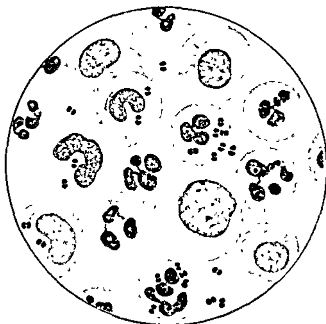


Fig. 2.—Cerebro-spinal fluid acute infection. (From a case of epidemic cerebro-spinal meningitis.)

PLATE 37.

Sleeping sickness.—A lymphocytosis occurs, but the only point of diagnostic value is the finding of the *Trypanosoma gambiense* in the fluid.

In encephalitis lethargica the fluid may contain no increase of cells, or a considerable mononuclear increase may be present, whereas **in poliomyelitis** and **polioencephalitis** there is usually a considerable cell increase.

Syphilis.—Sufficient reference has already been made to the cell and albumin changes in syphilis, and to the bearing of these and the Wassermann reaction on diagnosis.

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X-RAY DIAGNOSIS

By J. MAGNUS REDDING, F.R.C.S.

For accurate radiographic diagnosis it is necessary that certain fundamental principles be observed.

1. It cannot be too strongly urged that in the vast majority of cases screen examination alone is utterly insufficient for the formation of a definite diagnosis. In the examination of the respiratory and alimentary tracts fluoroscopy plays a highly important part, but even here radiograms should invariably be obtained in addition. Injuries of bones, even when the bone is large and superficial, may be, and frequently are, quite indistinguishable on the screen; while should the injury be recognized by fluoroscopy, further valuable information is generally obtained from a radiogram, which also forms a permanent and indisputable record of the condition.

2. An opinion should only be given on a radiogram of good quality, the result of complete elimination of movement on the part of the patient and of correct radiographic technique

3. Whenever practicable, two views at right angles should be obtained.

4. The views should be obtained according to a definite plan for every part of the body, so that the radiologist may be completely familiar with the normal appearance, and so be enabled to detect the slightest abnormality.

5. When two views at right angles cannot be secured, owing to splinting or the nature of the part examined—e.g. the shoulder or hip, stereoscopic radiograms are of considerable value; but stereoscopy should not be allowed to supersede the two-view technique.

6. It is the duty of the radiologist not only to interpret the radiograms, but also to estimate the value to be attached to this method of examination in any particular case. For example, it is possible to recognize or exclude a fracture in most parts of the body with absolute certainty, but the failure to demonstrate biliary calculi should not be allowed to influence the diagnosis in the slightest degree.

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Fig 1—Half vertebræ.

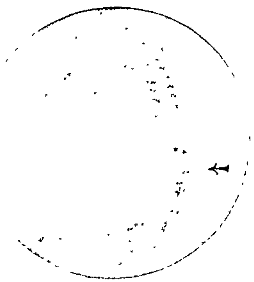


Fig. 2.—Spina bifida.



Fig. 3.—Cervical ribs

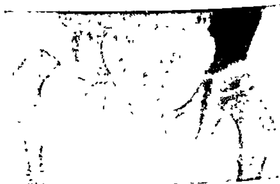


Fig. 4.—Congenital dislocation of hip.

PLATE 38.

I. THE SKELETAL SYSTEM

1. CONGENITAL AND DEVELOPMENTAL ABNORMALITIES

Examples are frequently met with of hypertrophy, reduplication, fusion, arrest of growth, and complete absence of bony structures; these conditions generally present no difficulties in diagnosis.

Where the nature of the lesion is not immediately evident, diagnosis depends on the exclusion of bony injury or disease.

The following abnormalities deserve special mention:

Fusion of two vertebræ is sometimes seen, generally in the lumbar region The four transverse processes are usually separate, the fusion affecting the bodies and articular processes. Complete bony continuity without any modification of structure is observed, but a lateral view is essential to exclude the possibility of an old compression fracture.

Half-vertebræ are most commonly seen in the dorsal region, where they frequently bear a supernumerary rib. They are often multiple. Diagnosis is made from the typical wedge shape of the vertebra, with or without supernumerary rib, and from the absence of any alteration in bony structure (Plate 38, Fig. 1).

Spina bifida.—The defect in the neural arches can usually be demonstrated in a lateral view of the spine (Plate 38, Fig. 2).

Cervical ribs, when very large, may closely simulate the first dorsal ribs. The diagnosis is made from the recognition of the vertebra with which the rib is connected, and from the abnormal position of the anterior costal extremity, the first dorsal rib nearly always retaining its normal position in relation to the sternum (Plate 38, Fig. 3).

Lumbar ribs are frequently seen, but are of no clinical importance apart from a possible bearing on operations on the kidney.

Extra ossicles are very common in the foot, much less frequent in the hand. In the *foot*, the os trigonum tarsi at the postero-external angle of the astragalus, the os tibiale externum forming a separate bone for the tubercle of the scaphoid, the astragalo-scaphoid ossicle at the upper margin of the corresponding articulation, and the os vesalii external to the base of the 5th metatarsal, are all of frequent occurrence, and may give rise to great difficulties in diagnosis. They are generally, but by no means invariably, symmetrical.

In the *hand*, the os triangulare below the tip of the ulnar styloid process, and the os centrale, between the os magnum and the scaphoid, are the only extra ossicles observed with any degree of frequency.

Extra epiphyses are very common for the head of the first metatarsal and the bases of the second and third metatarsals; and similar conditions are not infrequent in the metacarpal bones.

The apex of the patella may be formed by a separate ossific centre, and this may persist as a separate bone throughout life; or union with the remainder of the bone may occur, in which case some degree of elongation of the patellar apex is observed

Congenital dislocations occur in the hip, knee, shoulder, and radio-ulnar joints. By far the most common site of this malformation is the *hip* (Plate 38, Fig. 4). In this condition the acetabulum presents varying degrees of defect, from slight diminution in depth to almost complete absence. The head of the femur is displaced upwards, and frequently shows some degree of deformity, especially in older patients. The neck of the femur is frequently distorted. The displacement of the head of the femur is generally immediately apparent, but a useful check to diagnosis is provided by Shenton's line. This line is formed by continuing the lower border of the neck of the femur and the upper margin of the obturator foramen. In a normal subject the continuation of these borders will meet to form a gentle, regular curve. Should any displacement of the head of the femur, or any deformity of the neck, be present, the continuation of the two borders will meet at an angle.

In examination after attempted reduction of these dislocations, the hip is commonly found to be in Lorenz's position, the femur being *flexed, externally rotated, and abducted (Plate 39, Fig. 1)*; *Shenton's* line is not then available. The determination of complete reduction in these circumstances depends upon the position of the epiphysis of the head of the femur The centre of the epiphysis should be opposite the centre of the floor of the acetabulum, this being clearly defined in young subjects as the centre of the Y-shaped epiphysial cartilage (Plate 39, Fig. 1).

Congenital dislocations of the shoulder are rare, and may be combined with other bony abnormalities of the upper extremity. The head of the humerus is generally displaced downwards, and the acromion process of the scapula is curved down over the glenoid cavity like a hook (Plate 39, Fig 2).

Congenital dislocations of the *knee* are very rare, as are those of the *radius* and *ulna* Unless these conditions are seen in early infancy *it is hardly possible to exclude a postnatal traumatic lesion.*

To **multiple enchondromas** have been ascribed certain cases in which arrest of growth has occurred in all the long bones of one limb (Plate 39, Fig. 3) The radiographic appearances offer no support to this theory; the changes seen are those of complete irregularity of ossification, most marked in the extremities of the bones affected, but there is no evidence of chondroma or other new growth. *(See New Growths of Bone, p. 664.)*

Achondroplasia. — In this disease there is a remarkable



Fig. 1.—Reduced congenital dislocation of hip.



Fig. 2.—Congenital dislocation of shoulder.



Fig. 3.—Tibia and fibula in stunting of one limb.

PLATE 39.



Fig 1—Achondroplasia in an infant.



Fig. 2—Achondroplasia in a child æt. 15.



Fig. 3—Osteogenesis imperfecta.

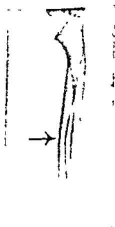


Fig 4—Green stick fracture

PLATE 40.

modification in the process of ossification of those epiphyses which appear before the sixth month of fœtal life. The growth in length which normally takes place at the epiphysial cartilage is suppressed, the epiphysial cartilage remaining inactive, and sometimes being replaced by fibrous tissue. Subperiosteal bone-formation is not affected. The radiographic appearances of this disease in infancy show but little variation from the normal. The epiphysial cartilages of the affected bones are seen to be diminished in depth as compared with those of a normal subject; the opposing aspects of the epiphysis and diaphysis may show slight increase in density; and the extremities of the diaphyses are commonly expanded, owing to relative excess of subperiosteal bone-formation (Plate 40, Fig. 1).

These changes are frequently so slight that great caution must be exercised in making a definite diagnosis. In the later years of childhood the radiographic appearances are very typical. The shafts of the affected bones are short and broad. There is generally some irregularity of the bony architecture, with isolated subperiosteal overgrowths, producing nodular projections. There is frequently some degree of curvature. At the extremity of the diaphysis the subperiosteal overgrowth is commonly well marked, and the epiphysial aspect of the diaphysis is dense and compact. The epiphysial cartilage is very narrow, or may have disappeared completely (Plate 40, Fig. 2).

The epiphysis itself is of normal size, but frequently shows some deformity due to irregular subperiosteal bone-formation

Osteogenesis imperfecta.—This disease is characterized by the occurrence of multiple antenatal and postnatal fractures. The bones show general rarefaction, with diminution in width of the compact layers, and frequently multiple cystic areas in the cancellous portion. The fractures unite rapidly, often with considerable deformity. The callus formed at the union appears normal, and the actual growth in length of the bones is unaffected (Plate 40, Fig. 3).

In adult life the bony structure tends to assume a normal appearance, modified by the old fractures with their resulting deformities.

2. INJURIES OF THE SKELETAL SYSTEM

Fractures.—In the majority of situations the presence of a fracture, its extent (incomplete, complete, comminuted), and the degree of displacement produced, can be demonstrated with certainty by means of radiograms obtained in two planes at right angles, or, wherever this is impossible, by stereoscopic radiograms. Often, however, fractures of the base of the skull cannot be demonstrated, and it may be impossible to exclude a fracture of a rib which is unaccompanied by displacement.

It must be emphasized, even at the cost of repetition, that screen examination alone is utterly useless as a means of excluding the presence of a fracture.

In young subjects, fractures, whatever their type, are frequently incomplete. Common examples are shown in Plate 40, Fig. 4 (greenstick fracture) and Plate 41, Fig. 1 (crush fracture of the radius, analogous to the Colles's fracture of the adult). The diagnosis that a fracture is incomplete depends on the recognition of bony continuity across some portion of the area involved, and this may only be evident in one of the two views obtained Incomplete fractures are not very common in adults, but are sometimes produced by direct violence. Incomplete fractures unaccompanied by any displacement are very easily overlooked unless a detailed examination of the radiogram be made. Complete fractures form the bulk of the injuries to the skeletal system of the adult. Generally they are readily recognized or excluded, but a comprehensive knowledge of normal appearances at all ages, and of developmental abnormalities, is essential for the avoidance of occasional errors. Plate 41, Figs. 2, 3, 4, and Plate 42, Figs. 1, 2, 3, 4, illustrate some common fractures

In estimating the degree and importance of displacement of a fracture, it must be remembered that any displacement is slightly exaggerated in a radiogram.

"Spontaneous" fractures may occur in old age, in the insane, and possibly in chronic alcoholism. In these general conditions no abnormality is seen to account for the fracture apart from some degree of rarefaction, which will be present in all the bones.

Spontaneous fractures may also take place as the result of disease of bone, either localized or generalized, e g. neoplasms, inflammatory lesions, and occasionally osteitis deformans The diagnosis rests upon the recognition of the alteration of bony structure produced by the primary lesion.

Union of fractures.—The greatest caution must be exercised in expressing an opinion on the degree of union present from X-ray appearances alone In young subjects bony callus may be quite obvious within a week of the injury, as an ill-defined opacity around the fragments, possessing no lamellar structure At the same time, the structure of the ends of the fragments becomes blurred and irregular. If the patient be examined at regular intervals, it will be seen that the opacity around the site of injury becomes more dense *and clearly defined*, and laminated in structure; and eventually a well-formed bridge of bone, continuous with the fragments, is demonstrated. Union by subperiosteal bone is generally obvious long before any osseous connexion between the opposing ends of the fragments is seen.



Fig 1—Crush fracture of radius.



Fig 2—Fracture of skull

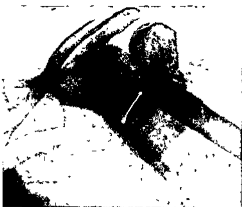


Fig 3—Fracture of surgical neck of humerus



Fig 4—Intracapsular fracture of neck of femur

PLATE 41

of the *semilunar bone* ranks second in frequency among the injuries of the carpus. The bone may be displaced completely forwards, but more commonly rotation takes place around the tranverse axis, the inferior concave surface being dislocated from the os magnum, and coming to look directly forwards. The injury is unmistakable in a lateral view (Plate 43, Fig. 3). Stereoscopic antero-posterior views cannot be relied upon for a diagnosis.

In the lower extremity the *hip-joint* is occasionally the site of traumatic dislocation The displacement of the head of the femur from the acetabulum can hardly be overlooked, but careful examination should be made for a fracture of some part of the acetabular rim, which, if present, may influence replacement.

Dislocation of the *knee* is very rare. (For dislocation of the patella, *see* Recurrent Dislocations below.)

The *ankle-joint* is frequently dislocated in conjunction with fractures of the malleoli. Gross displacements are commonly backwards, but minor lateral deviations are often seen in Pott's fracture, and should be carefully noted. Dislocations of the *vertebral column*, unless rapidly fatal, are frequently incomplete, and require antero-posterior and lateral views of the best quality for their recognition. Special attention must be paid to the articular processes and the spaces between the vertebral bodies. At the lumbo-sacral junction a displacement forwards of the 5th lumbar vertebra sometimes occurs (spondylolisthesis) due to exaggerated flexion, the inferior articular processes of that vertebra slipping over the articular processes of the sacrum on one or both sides. The condition is of particular interest in that the symptoms do not at first indicate the severity of the lesion, the patient gradually becoming more incapacitated owing to the increasing displacement which takes place. A lateral view of the lumbo-sacral region reveals the nature of the injury.

Recurrent dislocations.—X-ray examination does not usually demonstrate any bony abnormality to account for these conditions. Recurrent dislocations of the patella are generally associated with genu valgum. In longstanding cases osteo-arthritic changes may be seen in the affected joint, as after any form of articular trauma.

Epiphysial separation is quite a rare injury, the majority of cases which have been so designated being in reality juxta-epiphysial fractures of the diaphysis The only epiphysial separations which are seen with any degree of frequency are backward displacements of the lower epiphyses of the radius and ulna, either singly or in conjunction (Plate 44, Fig. 1), and abduction of the lower epiphysis of the tibia. Separations of the lower epiphysis of the femur, upper epiphysis of the humerus, and epiphysis for the head of the radius rank next in frequency.



Fig. 1.—Dislocation of shoulder with small fracture



Fig. 2—Dislocation of outer end of clavicle



Fig. 3—Dislocation of semilunar bone

PLATE 43.

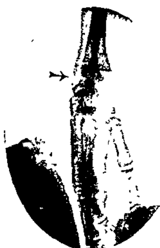

Fig 1.—Backward displacement of lower radial epiphysis.


Fig 2.—Coxa vara (slipped epiphysis)


Fig 3.—Coxa vara (infantile type)

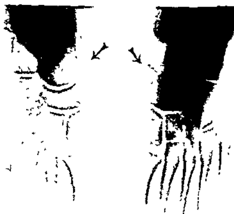

Fig 4.—Bilateral os tibiale externum (unilateral irritation)


Fig 5.—Schlatter's disease


Fig. 6.—Traumatic myositis.

PLATE 44.

The "slipped epiphysis" of the head of the femur, producing one of the forms of coxa vara (Plate 41, Fig. 2), probably belongs to a separate category. This condition arises apart from any very definite trauma, can be observed to take place gradually, and is apparently in the nature of a spontaneous separation resulting from some underlying disorder, to the pathology of which the X-ray appearances afford no clue. Coxa vara of the infantile type is shown in Plate 44, Fig. 3.

Minor injuries of the skeletal system.—Epiphysial irritation is not uncommon in children as a result of direct pressure or muscular over-action. Into this category fall the "tender heels" resulting from undue strain imposed upon the epiphysis of the os calcis by the tendo Achillis, and the tenderness which may develop over the tubercle of the scaphoid when this part is formed by a separate ossific centre. The affected epiphysis is seen to be increased in size, blurred and irregular in structure, and sometimes slightly fragmented. Plate 44, Fig. 4, shows bilateral epiphyses for the tubercle of the scaphoid, one of which has undergone the changes typical of irritation.

Schlatter's disease of the tubercle of the tibia closely approximates to the conditions described above Very often, however, the injury is produced by a single excessive contraction of the quadriceps extensor, and the tubercle is then seen to be slightly separated from the underlying head of the tibia; later the irregular new-bone formation and loss of structure typical of epiphysial irritation become apparent (Plate 44, Fig. 5) It was formerly stated that this lesion occurred only when the tubercle of the tibia possessed a separate centre of ossification, but this is incorrect.

Traumatic myositis ossificans may occur as the result of a fracture. In its most characteristic form, however, this condition is seen in the brachialis anticus and crureus muscles, following on apparently trivial injuries (Plate 44, Fig 6). The radiogram reveals an area of ossification close to, but definitely separated from, the injured bone. At first the new bone appears as an ill-defined, amorphous opacity, but later the structure becomes perfectly defined and the lamellæ are then seen to be parallel to the long axis of the shaft. It is only when every part of the new formation shows this definite lamellar structure, with clearly marked margins, that the disease can be stated to be quiescent.

Periodic examinations during the course of treatment frequently show progressive absorption of the new bone.

Traumatic periostitis.—For some days after the injury no X-ray changes will be observed, and should the subperiosteal effusion be quickly absorbed the lesion may never be demonstrated

radiographically. Usually, however, mineral salts become deposited in the raised periosteum, which is then seen as a thin curved linear opacity, blending at either extremity with the shaft of the bone. At a later stage new-bone formation may be seen, and this is commonly sclerosed, the sclerosis often also affecting the underlying cortical layer of the shaft. When the condition is first seen at this stage it may be impossible to exclude an old inflammatory lesion, but the very localized nature of the bony changes should render the diagnosis reasonably certain in the majority of cases

3. INFLAMMATORY LESIONS OF BONE

The changes which take place in bone as a result of inflammation are, with certain notable exceptions, well portrayed in a series of radiograms obtained during the course of the disease. It must be borne in mind, however, that inflammatory lesions in their earliest stages produce no recognizable variation from the normal X-ray appearances.

Some of the more common organisms involved in bone inflammations tend to produce characteristic X-ray changes, but in a great many cases the radiographic appearances are not sufficiently typical to warrant a definite diagnosis of the infecting agent.

Pyogenetic infections.—For the first few days of an acute **pyogenetic osteo-myelitis** no abnormality is discerned in the radiogram. The earliest change that can be made out is a slight rarefaction of bone, generally widespread, but more intense in one area, this corresponding to the original site of infection At the same time there is some blurring in detail of the bony structure. As the lesion progresses the rarefaction and blurring of structure will be seen to become irregular in distribution, some areas retaining fair density, while in others the bone shadow becomes very faint or entirely absent (abscess-formation).

The bony structure around these areas of advanced destruction is very indistinct.

The periosteum will generally be visible as a linear opacity separated from the shaft by a small interval, and the superficial layers of the cortex are often irregular and rarefied as a result of superficial necrosis. These changes are always widespread in an acute pyogenetic osteo-myelitis.

As the disease becomes less acute, formation of new subperiosteal bone is seen; this new bone is irregular in density and structure, and tends to be excessive in amount (involucrum-formation).

The underlying shaft shows very varied changes. Irregular abscess cavities and areas of superficial necrosis are seen to be interspersed with areas of sclerosis, which may become exceedingly dense

in the later (chronic) stages of the infection. In addition, there may be seen one or more dense opacities showing no definite structure, separated from the adjacent bone by an area of necrosis. These opacities represent sequestra, and can be readily recognized unless entirely enclosed by very sclerotic bone. *Unfortunately*, sequestra do not always acquire this increased opacity; sometimes the mineral salts are absorbed instead of being deposited in excess, with the result that the dead fragment becomes increasingly translucent to radiation, and may easily escape detection. In cases where the disease becomes chronic the radiogram shows widespread dense sclerosis, irregular in distribution; much new-bone formation of irregular structure; and frequently multiple abscess cavities, one or more of which may contain sequestra.

Pyogenetic arthritis is generally secondary to infection of adjacent bone, but may affect the synovial membrane primarily, e.g. in pyæmia, or in direct extension from wounds. The articular surfaces show widespread necrosis, and the cartilages are destroyed, this being evident from the approximation of the bones forming the articulation. If healing takes place, bony ankylosis very commonly results, complete continuity of bony structure being seen between the articular extremities.

To sum up, the X-ray appearances which differentiate a pyogenetic from other infections are the very *widespread* and very *irregular* nature of the bony changes seen at all stages of the disease; and in the later stages, the excessive irregular sclerosis and new-bone formation (Plate 45, Fig 1)

Tuberculous infections.—Very early tuberculous infections, like all other infections at the same stage, provide no radiographic data for diagnosis. Later, it is usual to see a rather localized general rarefaction of bone with loss of detail, the latter phenomenon being much more conspicuous than the former.

The most common type of fully developed tuberculous osteitis presents the appearance of a purely destructive inflammatory lesion. Extensive necrosis and abscess-formation are commonly seen in advanced disease, but the actual area of bone involved is comparatively small. For example, the head and neck of the femur may be almost entirely destroyed, while the upper end of the shaft shows little if any abnormality—a state of affairs never met with where pyogenetic infection has caused such extensive destruction. New-bone formation in this type is also very slight or even absent, at any rate until the healing process is well advanced (Plate 45, Fig. 2).

This is the type of tuberculous disease so commonly seen commencing on the diaphysial side of the epiphysial line of the long bones, and subsequently involving the adjacent articulation, the articular

extremities then undergoing destructive changes exactly similar to those around the primary focus (Plate 45, Fig. 3). It is this form of the disease also which is invariably seen in tuberculosis of the vertebral column.

In lesions of this type, the onset of healing is heralded by an improvement in structural detail. The healed lesion may show a moderate degree of sclerosis of fairly regular distribution, and a little new-bone formation, this commonly being compensatory rather than excessive, while the bone structure, although possibly irregular, is everywhere perfectly defined.

If the focus of disease is primarily in the synovial membrane, the bony changes, when they occur, nearly always conform to this destructive type. It must be remembered that a synovial tuberculosis may not at any stage produce any radiographic abnormality beyond a general atypical rarefaction of the articular extremities and adjacent portions of the shafts.

The second type of tuberculous lesion, much less common than the destructive form described above but still frequently seen, is that which results in the clinical manifestation of tuberculous "spina ventosa." This form is generally seen in the metacarpals, metatarsals, and phalanges, and about the elbow-joint, frequently involving all the bones of that articulation; it also occurs as an isolated lesion of the long bones, especially the ulna. The radiogram shows subperiosteal new bone laid down in successive orderly layers Sometimes this is for a time the only abnormality seen, and the condition is then indistinguishable radiographically from syphilitic periostitis (see p. 663). In the typical tuberculous lesion a central abscess cavity indicates the primary focus of infection (Plate 45, Fig 4), and the appearance of this central lesion is rarely long deferred.

Pneumococcal infections. — Diffuse pneumococcal osteomyelitis is rarely seen, and cannot be distinguished from a pyogenetic infection. Pneumococcal periostitis is not uncommon in children; the radiogram shows an extensive periostitis, usually without erosion of the underlying bone, the thickened periosteum being separated widely from the shaft by subperiosteal effusion. New-bone formation is generally very slight, or entirely absent.

Acute pneumococcal arthritis generally presents no X-ray changes, although the joint may be filled with purulent fluid. Chronic pneumococcal arthritis produces changes very similar to, and sometimes indistinguishable from, those of a tuberculous infection. The changes are, however, usually confined more closely to the articular surfaces than in a tuberculous lesion.

Gonococcal Infection.—Non-suppurative gonococcal arthritis produces an extreme degree of rarefaction of the bone immediately



Fig. 1.—Pyogenetic osteomyelitis.



Fig 2.—Tuberculous osteitis (destructive type).





Fig. 3.—Tuberculous arthritis.



Fig 4.—Tuberculous osteitis (proliferating type).

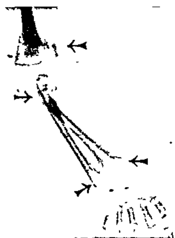


Fig 5.—Syphilitic epiphysitis.

PLATE 45.

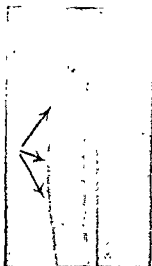


Fig 1.—Syphilitic periostitis.



Fig. 2.—Gummatous infiltration of bone.



Fig. 3.—Multiple chondromas.

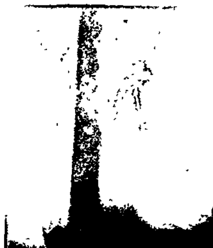


Fig 4.—Pedunculated exostosis.

PLATE 46.

below the cortical articular layer, the articular surfaces generally remaining intact. Suppurative arthritis of gonococcal origin cannot be distinguished from similar lesions due to other organisms.

Syphilitic disease of bone presents a wide diversity of radiographic appearances.

Congenital syphilis frequently manifests itself as an epiphysitis in infants. The opposing surfaces of the epiphysis and diaphysis are eroded, and show in consequence great irregularity and destruction of bone. The epiphysis itself is frequently displaced. An extensive periostitis is generally seen, the thickened periosteum being most widely separated in the immediate vicinity of the epiphysial cartilage (Plate 45, Fig. 5).

The synovitis which occurs in early puberty in congenital syphilis *provides no characteristic radiographic changes, a general rarefaction of bone being the only abnormality seen.*

The following manifestations of syphilis in bone occur in both the congenital and the acquired disease.

1. **Chronic periostitis.**—This is commonly seen in the humerus, ulna, femur, tibia, and frontal bones The condition extends over a wide area, and, in the long bones, frequently produces a regular spindle-shaped swelling due to successive layers of subperiosteal new bone. The regular nature of the periostitis, and the absence of *destructive changes in the underlying bone in such an extensive lesion,* are typical of a syphilitic infection (Plate 46, Fig 1).

2. **Localized gumma.**—In the early stages this lesion produces a localized destruction of bone with no well defined limitations, which may be indistinguishable from the appearance of an endosteal sarcoma. Careful examination will generally reveal a localized periostitis, the raised and thickened periosteum being visible as a faint linear opacity without definite new-bone formation Such a periostitis is strongly indicative of an inflammatory lesion, but it must be remembered that subperiosteal *new-bone formation* is an occasional concomitant of slow-growing endosteal sarcoma When localized gumma occurs in a long bone, a point of considerable importance in the differential diagnosis is that it usually produces a destruction of bone uniform in all directions; while an endosteal sarcoma tends to destroy cancellous bone more rapidly than the compact layers, and as a result the central portion of the shaft is seen to be involved over a wider area than the cortex

3. **Diffuse gummatous infiltration.**—In the active stages this condition produces a widespread very irregular destruction of bone with formation of new bone which is also irregular Areas of sclerosis are seen in the later stages only. Plate 46, Fig. 2, shows the characteristic "worm-eaten" appearance produced by this lesion.

The late results of localized or diffuse gummatous disease manifest themselves as sclerosis and hyperostosis, often extreme in degree, so that occasionally the bony structure is completely obscured. The sclerosis of syphilis is particularly prone to encroach upon the medullary canal. It is generally far more regular than the sclerosis of pyogenetic or tuberculous infections, but in many cases of old sclerosis and hyperostosis it is impossible to offer even a tentative diagnosis of the infective organism.

Post-typhoidal infections.—The characteristic post-typhoidal lesion shows a very chronic periostitis with regular new-bone formation; in the centre of the new bone is an abscess cavity with well-defined margins and very little surrounding sclerosis. Much less commonly a rather localized osteo-myelitis or an atypical periostitis is found to be post-typhoidal in nature, but these cases afford no radiographic clue to their origin

Miscellaneous infections.—The arthritic conditions which occur in association with scarlatina, measles, dysentery, etc., show no characteristic X-ray appearances. General rarefaction is frequently the sole abnormality.

If suppuration supervenes, the appearances do not differ fundamentally from those of a pyogenetic arthritis, but the inflammatory changes are usually more confined to the neighbourhood of the articular surfaces.

4. NEW GROWTHS OF BONE

(1) **Benign.**—*The majority of benign new growths of bone are chondromata or osteomata.*

Chondromas are frequently multiple, and then commonly occur in the hands. The affected bones show striking deformity in outline, and are much altered in bulk The bony margins are, however, perfectly defined, and the structure is normal (Plate 46, Fig. 3). A less common type, the enchondroma, appears in the medulla, and expands the shaft even to the point of fracture, but here again the margins of the affected area are well defined. This form of chondroma cannot be distinguished radiographically from a cyst of bone. Large ossifying chondromas occur in connexion with the bones of the pelvis. Owing to the density of the part, such a growth may closely simulate a periosteal sarcoma; if sufficiently good detail can be obtained, the absence of erosion of the underlying bone will establish the diagnosis (Plate 47, Fig. 1).

The **cancellous osteoma** presents the structure of normal bone, mostly cancellous, but sometimes possessing a thin cortical layer more compact in nature (Plate 46, Fig. 4). The pedunculated exostosis in the neighbourhood of an epiphysial junction often shows at the periphery a zone of irregular calcification, forming a cap to the



Fig 1.—Ossifying chondroma of pubes.



Fig 2—Endosteal sarcoma.



Fig. 3—Endosteal sarcoma.

PLATE 47.

lying cortex is plainly seen, and eventually the whole thickness of the bone may be eroded, the new-bone formation also being destroyed. In this advanced stage of the disease it may be impossible to differentiate the endosteal from the periosteal type of growth. Diagnosis otherwise is generally easy (Plate 48, Fig. 2), but occasionally, in chronic inflammation of the periosteum and underlying cortex, new bone is laid down in lamellæ radiating from the shaft; in these cases, however, the bony spicules do not possess the fine delicate character of those seen in sarcoma, and other changes indicative of an inflammatory lesion (e g sclerosis) can generally be recognized. Very rarely a periosteal sarcoma is encountered in which new-bone formation is absent. The radiogram then shows a purely destructive lesion, as in the endosteal growth, the destruction, however, being more evident on the surface of the cortex than in the deeper portions of the bone

Secondary carcinoma.—Secondary carcinomatous deposits in bone present a wide diversity of X-ray appearances. Commonly, a purely destructive lesion is seen very similar to endosteal sarcoma, but often to be distinguished from that condition by the presence of multiple foci of disease, separated by areas of fairly normal bone (Plate 48, Fig. 3). In other cases the deposits are very widespread, and the appearances are strikingly similar to those of osteo-myelitis, but inflammatory reaction is absent (Plate 46, Fig. 1). Very rarely the destructive changes are accompanied by new-bone formation, which may be excessive, and sometimes even shows sclerosis. Such a condition presents great difficulties in diagnosis unless taken in conjunction with clinical evidence

Secondary sarcoma is usually indistinguishable from primary endosteal sarcoma. Sometimes, however, the most noticeable feature is an increased density of the affected bone. This type is generally seen in the spine, where one vertebra may show a uniform increased opacity. Destructive changes may be quite masked for a time, but later become evident.

Myeloma produces a central and progressive destruction of bone, which is, however, always limited by well-defined margins of normal bony structure The destructive changes are accompanied by so-called "expansion," i.e. orderly formation of new subperiosteal bone, which for a time keeps ahead of the destruction. The X-ray appearances are therefore strikingly similar to those of a simple cyst, and frequently the two conditions cannot be differentiated. Two points are of value in diagnosis between these conditions: (a) In myeloma expansion is generally well marked in relation to the extent of the disease in the long axis of the bone, so that the translucent area tends to be spherical. In simple cyst, extension in the long axis is usually much in advance

of expansion. (*b*) Bony trabeculæ in the cavity are more common in myeloma.

In the later stages of myeloma the bony shell surrounding the growth is frequently seen to be destroyed at one or more points, and spontaneous fracture is common. (Plate 49, Fig. 1.)

Cysts of bone.—Cystic appearances may be seen in many general bone diseases, e.g. rickets, osteomalacia, osteogenesis imperfecta. These appearances are due to a localized excessive absorption of the opaque salts of bone, and are not indicative of true cyst-formation.

Fibro-cystic disease is commonly found in the upper ends of the humerus and femur in children and young adults. The X-ray appearances are those of a localized central destruction with well-defined margins and no surrounding bony change. Expansion is less common than in myeloma, and spontaneous fracture very frequently takes place before any great deformity in the external configuration of the bone is seen. (Plate 49, Fig. 2.) Bony union is the rule, and sometimes the cystic cavity becomes partly filled with new bone after such a fracture Periodical examination will, however, generally show eventually a renewed extension of the disease. The X-ray changes give no indication of the nature of the cyst contents, which may be either solid or fluid, but they form a very definite indication of the innocence of the lesion, all the more valuable in that the histological appearances are very varied and frequently anomalous.

Hydatid cysts of bone are often multilocular. When they occur in the long bones, differentiation from other cysts is not possible radiographically When occurring in the spinal column, they may lead to a simple collapse, usually limited to a single vertebra. similar to that seen in secondary carcinomatous deposits

5. DISEASES OF DOUBTFUL PATHOLOGY

Osteo-arthritis. — A diagnosis cannot be made prior to the formation of osteophytes. These are seen at the margins of the articular surfaces, and are smooth and regular in outline, showing the structure of normal compact bone. They may attain a considerable size (Plate 49, Fig. 3). At a later stage, new-bone formation may be seen in the region of ligaments, and calcification or ossification sometimes occurs in intra-articular structures, calcification being not uncommon in the articular cartilages. Erosion of articular cartilage can be recognized in advanced cases by reason of the approximation of the articular extremities, and when this has taken place some condensation and irregularity of the adjacent cortical bone may be seen. Primary osteo-arthritis is remarkable for the complete localization of the bony abnormality to the articular surfaces; secondary

osteo-arthritic changes are, however, often seen in joints which have been damaged in any way—e.g. by intra-articular fracture or infective arthritis—and in such cases the appearances may be complicated by those of the primary lesion. Bony ankylosis never occurs in osteo-arthritis.

In **spondylitis deformans** the X-ray appearances are very similar to those of osteo-arthritis, with the important difference that, in spondylitis, bony ankylosis between one or more vertebræ commonly occurs: new-bone formation is also seen around the non-articular aspects of the vertebral bodies (Plate 50, Fig. 1).

Polyarticular rheumatoid arthritis.—The changes typical of this condition are always best seen in the hand and wrist (Plate 49, Fig. 4). They are:

(1) Rarefaction of the articular extremities.

(2) Small rounded areas of translucency involving the margins of the articular surfaces, and having a "punched-out" appearance.

(3) Small, irregular, spiky. bony outgrowths of cancellous structure at the articular margins, quite unlike the smooth rounded osteophytes of osteo-arthritis. (As pointed out above, however, secondary osteo-arthritis may supervene in a joint damaged by rheumatoid arthritis.)

(4) Approximation of articular surfaces due to destruction of cartilage, and, later, erosion of the articular surfaces. This may be so marked in the carpus that differentiation between the individual bones is lost.

(5) In advanced cases, subluxation and dislocation of the metacarpo-phalangeal and inter-phalangeal joints.

Bony ankylosis is sometimes seen in joints of which the cartilage and underlying cortex have been eroded.

Still's disease.—The joint changes in this disease are similar to those of rheumatoid arthritis, but are seldom pronounced. The carpus constantly shows a degree of ossification in advance of that normal to the age of the patient, and for some time this phenomenon, combined with some general rarefaction, may form the only radiographic abnormality. This advanced ossification is not, however, peculiar to Still's disease, but is commonly seen in any chronic inflammatory disease involving growing bones and epiphyses.

Hypertrophic pulmonary arthropathy.—The typical X-ray appearances of this disease are produced by the formation of subperiosteal new bone, best seen around the shafts of the metacarpals and phalanges (1st and 2nd rows), but also occurring around the other long bones near their articular extremities Articular changes may be entirely absent. If present, they are similar to those of rheumatoid arthritis.





Fig. 1.—Myeloma of ulna.

Fig. 2.—Fibro-cystic disease of humerus.



Fig. 3.—Osteo-arthritis of knee: opaque bodies in joint



Fig. 4.—Rheumatoid arthritis.

PLATE 49.

whether this disease actually occurs in infants; if it in fact does so, it cannot be distinguished radiographically from *osteogenesis imperfecta*.

Osteitis deformans (Paget's disease).—Two distinct stages, early and late, can be *recognized in this disease*. *In the early stage*, which may persist for years, diffuse irregular absorption of lamellæ is seen in the affected bones. This absorption involves the cancellous and compact layers equally, and in the long bones tends to spread in the long axis of the shaft. In the skull the absorption is quite irregular. (Plate 51, Fig. 1.) The earliest incidence of the disease is generally in the tibia, femur, pelvis, and lumbar spine, in that order of frequency. The bones of the vault are usually affected at a much later stage.

The absorption is accompanied by—(1) New subperiosteal bone-formation, with resulting increase in girth; the new bone is, however, subjected to lamellar absorption almost as soon as it is formed. (2) Irregular calcification of both new and old bone, so that the detail is blurred throughout (Plate 51, Figs. 2, 3). In this stage of the *disease curvatures occur in the long bones and vertebral column, and* spontaneous fractures are sometimes seen. In the later stages of the disease, excessive deposit of mineral salts occurs throughout the altered tissues, and the bone presents a densely opaque and completely structureless appearance (Plate 51, Fig. 3). Instances of this disease affecting one bone only (practically always the tibia) are not uncommon as judged by clinical observation; X-ray examination will, however, nearly always demonstrate that similar changes are present in other parts of the skeletal system.

Osteitis fibrosa.—The relation of this disease to fibrocystic disease on the one hand and osteitis deformans on the other is at present obscure. In osteitis fibrosa bone is replaced by *longitudinal striæ of fibrous tissue; new subperiosteal bone is formed*, producing increase of girth, and this is similarly affected by *lamellar absorption*. The X-ray appearances are very similar to those of osteitis deformans in its early stage, but differ in the following details:

(1) In osteitis fibrosa the replacement of bone is very much more extensive, *producing wide translucent areas;* definite cysts are often thus formed.

(2) Osteitis fibrosa may affect many bones, but is often quite localized, *the transition to normal bone being abrupt*.

(3) The affected area does not show the blurring of detail which is characteristic of osteitis deformans.

(4) Small localized *areas of densely sclerotic bones are frequently* present. Fig. 1, Plate 52, demonstrates most of these points, and should be compared with Fig. 2, Plate 51.



Fig. 1.—Osteitis deformans of skull.

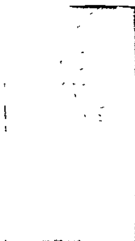


Fig. 2.—Osteitis deformans (early).



Fig. 3.—Osteitis deformans (late).

PLATE 51.



Fig 1.—Osteitis fibrosa.



Fig. 2.—Kohler's disease.

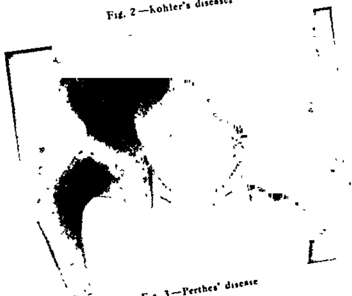


Fig 3.—Perthes' disease

PLATE 52.

Osteitis fibrosa has no late stage corresponding to that of osteitis deformans; the appearances do not alter as the disease progresses, unless sarcoma supervenes, in which case the characteristics of that affection will be noted.

Köhler's disease of the tarsal scaphoid bone.—In this condition the ossification of the scaphoid in the foot is diminished in extent, very irregular, and sclerotic. The X-ray appearances are those of a small, dense bone, irregular in shape, and frequently fragmented into several pieces. The normal space which remains between the head of the astragalus and the cuneiform bones shows, however, that the diminution in size is confined to the opaque elements of the bone. The disease is very frequently bilateral (although one foot only may give rise to symptoms), but is not symmetrical in the two feet. The more extensive changes may sometimes be seen in the foot which is clinically unaffected (Plate 52, Fig. 2).

The disease commonly occurs between the ages of 5 and 7 years. It has never been seen in a foot previously found to be normal, nor to get worse, subsequent examinations invariably showing the condition to be either stationary or improved. The return to normal is exceedingly slow, but is eventually complete.

Perthes' disease of the hip (*syn.* Legg's disease, Calvé's disease, Pseudo-coxalgia, Caput planum, Coxa plana, Osteochondritis juvenilis).—This disease occurs between the ages of 5 and 10 years. It is usually unilateral, but sometimes bilateral, in which case it is rarely symmetrical. In the early stages the ossific nucleus of the head of the femur is seen to be reduced in size and of increased density. Later the head becomes very definitely flattened, and spreads out beyond the upper border of the acetabulum, appearing to overlie the neck of the femur. The ossific nucleus of the head at the same time becomes fragmented, and the neck broad, sometimes with irregular areas of rarefaction in the neighbourhood of the epiphysial cartilage.

The great trochanter may show enlargement and some irregularity of bony structure.

Areas of rarefaction and irregularity of ossification are often seen in the acetabulum. The space between the acetabulum and the fragmented, flattened, ossific nucleus of the head is increased, showing that an abnormal width of unossified cartilage exists As healing takes place the fragmentation of the head of the femur disappears, and later the density of this part returns to the normal. The end-result is a large flattened femoral head extending beyond the confines of the acetabulum, and a short thick femoral neck; this condition persists throughout life.

Coxa vara, if it occurs, is never a marked feature of the deformity in this disease. It will be seen that the X-ray appearances of Perthes'



Fig. 1.—Osteophytic spur of os calcis.



Fig. 2.—Empyema of frontal sinus.



Fig. 3.—Empyema of right maxillary antrum.



Fig. 4.—Malignant neoplasm of antra.

PLATE 54.

Ossification extending into fasciæ and intermuscular septa, with no history of previous trauma, is not uncommon. The most important example of this condition is the calcaneal spur (Plate 54, Fig. 1). These formations may attain considerable size, are frequently bilateral, and are sometimes fractured as a result of trauma. They are generally seen in the later years of life, but may occur at any age in adults, and even in children. Ossification is also seen at times, extending into the origin and insertion of muscles and their tendinous extremities, as a result of a single or repeated muscular over-action. The new formation is of rather irregular cancellous structure, directly continuous with the bone from which it originates.

Traumatic myositis ossificans is described under Injuries to Bone (p. 659).

III. LYMPHATIC GLANDS

Normal lymphatic glands are not distinguishable on X-ray examination. Glands which have undergone considerable **enlargement,** as a result of inflammation, neoplastic deposits, blood diseases, etc., may show a definite opacity, but it is usually impossible to recognize the glandular origin of this shadow in situations other than the thorax. An exception to this rule is provided by glands which have become the seat of calcareous deposit (*see* below).

In the thorax a moderate enlargement of the bronchial glands is commonly seen in adults, and frequently in children also, but it is only when the enlargement is excessive, or the visible glands are very numerous, that the condition can be said to possess any pathological significance. Recognition of enlarged posterior mediastinal glands, on the other hand, always indicates an abnormal condition. These glands are seen by placing the patient in an oblique position. They are differentiated from other causes of abnormal opacity by their rounded outline, and absence of direct continuity with the heart and great vessels in front, or the spinal column behind. The relation of the opacity to the œsophagus must also be elicited by observing the passage of an opaque bolus. Enlargement of the aortic glands is usually the result of new growth. The X-ray appearances may very closely simulate those of aortic aneurysm (Plate 57, Figs. 2, 3); the differential diagnosis is discussed under the latter heading (p. 681).

Calcification of the lymphatic glands in any part of the body renders these structures visible on X-ray examination. The opacities presented by this condition vary with the extent to which calcification has occurred, but in general terms they are irregular in outline and density, and are definitely granular; they are commonly multiple. Some degree of calcification is usually seen in the bronchial

glands of the adult, and presents neither diagnostic difficulty nor pathological significance.

The demonstration of calcified abdominal glands may be of positive value in the diagnosis of obscure tumour-formations, and in suspected chronic inflammations of the appendix, in which condition the ileo-colic glands are sometimes calcified. More commonly, however, the radiologist is concerned with the differentiation of these glands from calculi in the urinary and biliary tracts.

The granular, irregular nature of the opacities will often suffice to make the diagnosis clear. In other instances, calcification has become so extensive that the characteristic appearances are lost. In such cases every effort must be made, by repeated examinations in different positions, to displace the opacity from the areas known to correspond on the radiogram with the urinary and biliary structures. Since the mesenteric glands are those commonly affected, this displacement is rarely a matter of any great difficulty.

IV. *THE RESPIRATORY SYSTEM*

1. THE UPPER AIR-PASSAGES

In a postero-anterior view of the skull the *nasal fossæ* are seen as somewhat pear-shaped translucent areas, with their broad bases below; separated by the mesial opacity of the *nasal septum*, and encroached upon laterally by the *middle and inferior turbinate bones. Deviations of the septum and hypertrophy of the turbinates are well* seen. The radiologist is more often concerned, however, with the accessory nasal sinuses, and these must be considered in some detail.

The *frontal sinuses* are seen as translucent areas having very clear-cut margins. They are often trefoil in form, but present great variations in shape and size, and are rarely symmetrical. Sometimes the infundibulum ends in a small rounded projection on one or both sides (rudimentary frontal sinus); sometimes the sinuses extend right across the orbit, and are seen in a lateral view to reach back into the horizontal plate of the frontal bone. A large frontal sinus rarely shows equal translucency over its whole extent. Since the sinuses depend to some extent for their translucency on the air which they normally contain, it follows that any condition which results in displacement of this air (e g. œdema of the mucosa, retention of secretion, or actual empyema) will produce some loss of translucency. In the frontal sinuses the variation from the normal appearances may, in recent cases, be very slight, and the difficulty of diagnosis is much increased by the common asymmetry of the two sinuses. When the pathological condition is of long standing, and especially

when suppuration has occurred, rarefying osteitis and necrosis of the bony walls of the sinus may become apparent, and these appearances, in conjunction with some diminution of translucency, are of great diagnostic value (Plate 54, Fig. 2).

The *ethmoidal sinuses* are seen on either side of the nasal fossæ as translucent areas divided by a number of fine bony trabeculæ (the walls of the individual air-cells). Inflammatory disease of these sinuses is shown by loss of translucency and by loss of bony structure in the outer wall and trabeculæ.

The *sphenoidal sinuses* can be seen in a postero-anterior radiogram of good quality, but their appearance is so obscured by the parts lying anteriorly to them that a definite opinion as to their condition is rarely possible. In a lateral view the sinuses are always well seen, but minor variations in translucency must be disregarded. Any considerable opacity as seen in this view, however, will enable a diagnosis to be made with some degree of confidence.

The *maxillary antra* are seen as roughly triangular translucent areas. They are, for practical purposes, symmetrical, and the presence of œdema of the mucosa or retained fluid always results in a recognizable loss of translucency. Œdema of the mucosa alone commonly results in a simple contraction of the translucent area, while retention of fluid will produce a uniform opacity of the whole antrum, and a distinction between the two conditions can thus frequently be made (Plate 54, Fig. 3). The possibility of bilateral empyema must not be forgotten in comparing the two sinuses.

From the above brief description it will be seen that the information obtained by X-ray examination varies in value in regard to the particular sinuses concerned. In general, it may be stated that definite positive findings are conclusive evidence of the presence of an inflammatory lesion (or, rarely, a neoplasm), in whatever sinus they occur. Failure to detect loss of translucency in the maxillary antrum is conclusive evidence of absence of such a lesion; in the ethmoidal sinuses normal translucency and good structural detail of bone carry considerable weight, but are hardly conclusive; while in the frontal and sphenoidal sinuses, failure to detect any abnormality, especially in cases of recent origin, may be completely misleading.

Osteomas involving the frontal sinuses and maxillary antrum present the same characteristics as similar growths elsewhere.

Malignant neoplasms originating in the nasal fossæ and maxillary antra (Plate 54, Fig. 4) produce the typical destructive changes described in Section I. In the early stages of the disease, however, it may be impossible to differentiate the condition from an inflammatory lesion of the sinuses involved.

2. LARYNX, TRACHEA, AND BRONCHI

The larynx and the cervical portion of the trachea are recognized in lateral views of the neck as translucent areas in virtue of the contained air. The laryngeal cartilages, especially the thyroid cartilage, are, moreover, commonly calcified to some extent in middle-aged and elderly subjects; this condition may prove misleading as seen in an antero-posterior view, as the opacities might be ascribed to an abnormality of the cervical spine; a lateral view will render the diagnosis clear.

Lateral deviation of the trachea, both in the neck and in the thorax, is usually well seen (Plate 55, Fig. 1). The intrathoracic portion of the trachea, and the bronchi, cannot be differentiated from the surrounding structures in a normal subject. Dilatation of a bronchus gives rise to an abnormal opacity or translucency according to the contents—fluid or air—at the time of the examination, but these appearances may be masked by changes in the surrounding lung. Opaque foreign bodies in the respiratory passages are readily seen unless very small, or in those cases where their continued presence has produced changes in the adjacent lung tissue. They are most commonly found to occupy the right bronchus, or one of its lower divisions.

3. LUNGS AND PLEURA

In the X-ray investigation of these structures it is of advantage to examine the patient both in the upright and in the supine position if this is possible. Screen examination plays an important part, but should always be followed by one or more radiograms taken with the breath held.

Preliminary screen examination should include the whole thorax. The diaphragm on the tube box should then be closed so as to limit the field of radiation to a transverse slit; this facilitates comparison of corresponding parts of the two lungs. Attention should first be directed to the apices, and any inequality in translucency duly noted. [illegible]

[illegible] entry. The lighting-up in the two apices should be equal in degree, or only slightly greater in the right apex. A similar examination is made of every part of the two lungs, special attention being paid to any area which appears abnormal.

When, at the end of this systematic examination, the diaphragm is brought into the field of illumination, the shape, position, and

movements of this structure on normal and on forced respiration must be carefully investigated. In normal subjects the position of the diaphragm undergoes constant variations with the respiratory movements, the usual degrees of excursion being about ½ in. in quiet, and 2–2½ in. in forced respiration. Variations in position are also produced by the condition of the stomach and intestines. Generally speaking, the upper limit of the right leaf of the diaphragm on forced expiration corresponds to the 4th costal cartilage in front, while the left leaf lies ½–1½ in. lower.

The radiographic appearances of the *lung structure* are best studied in a radiogram taken with the breath held. It will be seen that the normal lung presents numerous striate opacities radiating from the hilus, and becoming finer and more diffuse as the periphery of the organ is approached. These striæ are produced by the bronchi and bronchioli.

The translucency of the lung tissue is further modified by the shadows of smaller bronchioli the long axes of which correspond more or less with the axis of radiation; and these produce the uniform fine variation in light and shade which is known as the "normal lung mottling."

Fibrosis.—This may be localized or diffuse, unilateral or bilateral; it produces an increase of the radiating striæ with corresponding loss of translucency and of lighting-up on inspiration. Limitation of movement of the diaphragm and deformity of that structure are common, and displacement of the heart towards the affected side may be seen in unilateral lesions.

Inflammatory lesions.—Acute lobar pneumonia, seen in the stage of actual consolidation, produces a fairly dense, uniform opacity, limited to one or more lobes of the lung. There is no lighting-up on inspiration over the diseased area, and diaphragmatic movements are commonly diminished. In chronic (unresolved) lobar pneumonia the opacity becomes less complete and its margin less well-defined. Considerable fibrosis is generally seen, sometimes accompanied by displacement of the heart towards the affected side.

In acute broncho-pneumonia the radiographic appearances are not at first greatly modified. In the fully-developed phase of the disease numerous small opacities are seen scattered throughout the lung substance, and a general diminution of air-entry is noted. Failure of complete resolution is indicated by fibrosis.

Abscess of the lung, supervening in the course of an acute pneumonia, is frequently completely masked by the opacity of the surrounding tissues. Chronic lung abscess is seen as a rounded or irregular area of increased or diminished translucency according to the nature of the contents (fluid or air) at the time of examination.

Examination in the upright position may show a horizontal fluid level below an area of increased translucency. The cavity is always surrounded by a zone of fibrosis.

Pulmonary tuberculosis in the active state produces diminished air-entry, limitation of diaphragmatic movement, and groups of small rounded opacities with ill-defined margins. The distribution of these opacities may be apical, perihilar, or diffuse; if diffuse, the distinction from the broncho-pneumonia due to other organisms cannot be made by X-ray examination alone. Contributory evidence of tuberculosis may be afforded by the long, narrow shape of the thorax, with *steeply sloping ribs and very acute subcostal angle* (the phthinoid thorax), and by the small transverse diameter of the heart as seen in the upright position.

X-ray examination is of particular value in the perihilar type of tuberculosis, as well-marked changes are often observed long before the disease is manifest to other methods of investigation. In no cases of doubtful phthisis, however, can the absence of X-ray evidence be regarded as definitely excluding the presence of disease.

Advanced cases of pulmonary tuberculosis often present a variety of lesions. Large areas of consolidation, cavitation, and fibrosis may be seen in the regions longest affected; and groups of small rounded opacities will be observed in the more recently involved areas. In healed tuberculous disease the diffuse consolidation and small rounded opacities are replaced by fibrosis, which sometimes encloses areas of calcification. Air-entry improves, but is rarely restored to the normal. It is frequently impossible to state from the *X-ray examination alone that the disease is definitely healed.* (Plate 55, Fig. 2.)

Pleural effusion.—A small effusion is best seen on screen examination; it presents an opacity which occupies the costo-phrenic angle and possesses a well-defined crescentic free margin, concave upwards and inwards. The base of the opacity tends to obscure the diaphragm, the movements of which are diminished or even com*pletely arrested.* The shape and position of the opacity undergo very little if any change with alterations in the position of the patient. In the case of a larger effusion the opacity may blend internally with the shadow of the cardia, but the crescentic free margin is still retained; this is, however, always better seen on the screen than in a radiogram. It is never possible to make a diagnosis *as to the nature* of the fluid—i.e. whether serous or purulent.

Pleural thickening may closely simulate pleural effusion; in the former condition, however, the opacity is less well defined, the crescentic margin being replaced by a much more gradual transition to the normal translucency of the lung above the affected area; and



Fig 1—Deviation of trachea (fibroid phthisis).



Fig 2—Diffuse pulmonary tuberculosis

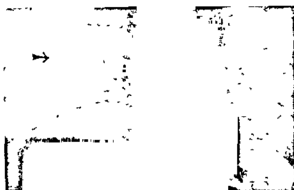


Fig 3—Hydropneumothorax

PLATE 55.



Fig 1 —Secondary carcinoma of lung.



Fig 2 —Mediastinal neoplasm



Fig. 3 —Hydatid cyst of right lung.

PLATE 56.

the diaphragm is less obscured than is commonly the case in effusion. Extensive pleural thickening may, however, effectually mask a small collection of fluid.

Pneumothorax.—The X-ray appearances in pneumothorax are very characteristic. The affected side of the chest shows greatly increased translucency, with complete absence of any sign of lung structure, and the collapsed lung is seen as a well-defined opacity applied to the heart and great vessels. The latter are displaced towards the unaffected side. In hydro- and pyo-pneumothorax (which cannot be differentiated from one another radiographically) the opacity of the effusion presents a horizontal upper margin when the patient is viewed in the upright position, this horizontal margin being retained on bending the patient from side to side. Shaking the patient will produce visible ripples on the surface of the effusion. Hydro- and pyo-pneumothorax will not be recognized if the patient is examined in the horizontal position only. (Plate 55, Fig. 3)

Cases of old **empyema**, with incomplete expansion of the lung, cause considerable difficulty, as the great pleural thickening commonly present may completely mask a small pneumothorax or collection of fluid; in fact, the X-ray examination of these cases is usually singularly barren of useful result

The presence of a **subdiaphragmatic abscess** may be indicated by examination of the thorax. The diaphragm on the affected side is elevated and immobile, and a small pleural effusion is often present. Since these appearances may result from pleural infection alone, clinical evidence of a lesion below the diaphragm is necessary to establish the diagnosis.

New growth of lung.—Innocent tumours of the lung are so rare as to call for no special mention. **Carcinoma** and **sarcoma** occur occasionally as primary growths of the lung, and have usually attained considerable size before coming to the radiologist. The tumour then presents a large, very dense, irregular opacity, with well-defined margins, and no surrounding lung changes. Enlargement of the bronchial glands will be seen in the later stages, and pleural effusion may be present; the latter may be closely simulated by a growth of the base of the lung.

Secondary carcinomatous and **sarcomatous** metastatic deposits are frequently seen. They produce multiple opacities of considerable size, the smallest being, as a rule, much larger than the opacities of tuberculosis; and they possess well-defined margins quite unlike those of inflammatory consolidations (Plate 56, Fig. 1). In a much less common form of metastatic deposit, known as carcinomatosis, the multiple opacities are very small, and the diagnosis from miliary tuberculosis is one of great difficulty. The

more clearly defined outlines of the neoplastic opacities will, however, generally enable a correct opinion to be given.

Sarcoma of the mediastinal glands commonly spreads eventually to one or both lungs, and then produces an opacity in the region of the hilus, similar to that of a primary growth of the lung The large mediastinal tumour points to the secondary nature of the lung involvement in these cases. (Plate 56, Fig. 2) *See also* under Lymphatic Glands (p. 673) and Cardio-Vascular System (p. 681).

Hydatid cysts of lung are rarely seen until they have attained a considerable size. The cyst then produces a large rounded opacity with perfectly defined regular margins. There is frequently an almost complete absence of change in the surrounding lung structure. Less commonly, a certain amount of fibrosis is seen around the cyst-wall (Plate 56, Fig. 3).

V. THE CARDIO-VASCULAR SYSTEM

1. THE HEART AND GREAT VESSELS

Screen examination is made in both upright and horizontal positions, the patient being rotated slowly from side to side while under observation; and fluoroscopy is followed by the taking of one or more radiograms. In this way it is possible to collect data as to the size, shape, position, and movements of the heart and great vessels.

The shape of the heart varies considerably in normal subjects in accordance with the shape of the thorax, and this variation modifies the cardiac diameters The greatest transverse diameter of the heart in the normal subject is 39–50 per cent. of the greatest transverse diameter of the bony thorax. A cardiac diameter of 53 per cent. or over indicates a definite enlargement. The plates from which these measurements are obtained are taken in the upright position, the breath being held in mid-inspiration. The X-ray tube should be 6 ft. from the plate, as at this distance distortion due to divergence of radiation is negligible.

It is usually possible to state which side of the heart is involved in any enlargement noted, but dilatation cannot be differentiated from hypertrophy. Localized irregularities in outline may be produced by pleuro-pericardial adhesions.

Minor variations in the shape and size of the heart have been described as characteristic of different cardiac lesions, but confirmatory evidence is required before these statements can be accepted.

The position of the heart can be mapped out on the thoracic wall with absolute accuracy. Displacement may be due to traction, or



Fig. 1.—Pericardial effusion.



Fig. 2.—Fusiform aneurysm.



Fig. 3.—Saccular aneurysm.

PLATE 57.

to pressure, on the viscus, and the causal factor (e.g. pleural effusion, fibroid lung) can usually be demonstrated radiographically.

Pericardial effusion, unless very small in amount, can be readily recognized. The cardiac opacity becomes enlarged and globular in shape; pulsation is diminished or lost; and the cardiophrenic space (a translucent area normally seen on inspiration between the diaphragm and the inferior aspect of the apex) is obliterated (Plate 57, Fig. 1).

Aneurysm of the thoracic aorta can usually be demonstrated. The opacity of the vessels may show a diffuse increase in width—fusiform aneurysm (Plate 57, Fig. 2), or a localized projection may be seen from some part of an otherwise fairly normal aortic shadow—saccular aneurysm (Plate 57, Fig 3). It is important to recognize the existence of a projection to the left, present in the normal subject, produced by the transverse portion of the aortic arch. This has been responsible for many erroneous diagnoses of aortic aneurysm. The differential diagnosis of aortic aneurysm from enlargement of the mediastinal glands due to neoplasm may present very great difficulty, both conditions being characterized by an opacity in the superior and middle mediastina. The following points should be considered:

(1) Aortic aneurysm often presents a regular rounded outline. The opacity due to enlarged glands is always irregular in outline.

(2) The opacity of aneurysm is frequently unilateral, that of enlarged glands is nearly always bilateral.

(3) It is occasionally possible to recognize expansile pulsation as an aneurysm.

(4) In aneurysm some part of the abnormal opacity is always found to be directly continuous with the aortic shadow. In glandular enlargement it may be possible to demonstrate an unbroken line of demarcation from the aorta.

(5) The left border of the heart is often unusually horizontal in cases of aneurysm. This observation is not, however, of great value

2. PERIPHERAL VESSELS

Calcification of peripheral vessels, especially the posterior tibial and peroneal arteries, is quite commonly demonstrated in elderly subjects.

Calcification sometimes occurs in nævoid tumours, and is seen as small rounded opacities in the soft tissues. Plate 58, Fig. 1, shows several of these, and also an area of myositis ossificans which followed partial removal of the tumour.

Aneurysm of vessels other than the thoracic aorta and its main branches cannot be recognized with any degree of certainty; the

opacity produced by the aneurysm, *if it can be distinguished at all* from that of the surrounding tissues, affords no indication of the nature of the lesion.

VI. THE ALIMENTARY SYSTEM

1. THE TEETH

Retained and misplaced teeth are readily demonstrated, the upper canines and lower 3rd molars providing the most common examples of these abnormalities.

The lower 3rd molar teeth are sometimes found in the ascending ramus of the mandible, and may be completely inverted; more commonly they are horizontal in *position, with the biting surface* of the crown impacted against the posterior wall of the second molar.

The 3rd molar teeth cannot be demonstrated radiographically until the twelfth year of life.

Acute inflammatory conditions in connexion with the teeth conform in general terms with similar lesions of bone elsewhere, but some special description is required of the chronic types of inflammation.

Chronic periodontitis is manifested in its early stages by rarefying osteitis and absorption of the alveolus forming the socket of the affected tooth. These changes are generally first apparent at the alveolar margin, and gradually extend to the deeper portions of the socket (Plate 58, Fig. 2).

It must be remembered that in elderly subjects a certain amount of absorption of the alveolus is normally present. But in this case the alveolus retains its horizontal margin between the teeth, there is no loss of detail in the bony structure, nor is there any absorption of the socket still remaining around the tooth—i.e. the X-ray appearances are normal, except that rather more of the tooth projects beyond the socket than in a younger subject.

"Pyorrhœa" may be a marked clinical feature in the complete absence of X-ray changes, and conversely X-ray changes are not always associated with the presence of demonstrable pus.

Chronic apical osteitis is seen as a rounded translucent area about the apex of the tooth (Plate 58, Fig. 3). In the early stages of the disease the margins of this area are ill defined, and some blurring of structure of the surrounding bone indicates the activity of the inflammatory condition. In the later stages the area of osteitis presents a clear-cut, slightly condensed margin, and the surrounding bone appears normal. *The teeth thus affected may provide no* clinical evidence of disease, but there is abundant evidence that apical osteitis is the result of bacterial infection in the vast majority of cases, if not *in all, and that X-ray changes suggestive of extreme* chronicity

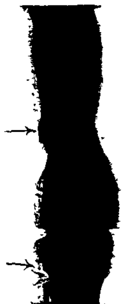


Fig 1—Calcification of nævoid tumour and myositis ossificans



Fig 2—Chronic periodontitis.



Fig 3—Apical osteitis.



Fig. 4—Salivary calculus



Fig. 5.—Pharyngeal pouch

PLATE 58

and inactivity are no indication that the condition is harmless to the patient.

2. SALIVARY GLANDS

Salivary calculi generally present somewhat indefinite opacities, rounded or irregular in shape if situated in the gland, elongated if the duct has been the site of formation (Plate 58, Fig. 4).

3. PHARYNX AND ŒSOPHAGUS

The position of the *pharynx* is well seen in a lateral view of the neck owing to the translucency of the air-contents The recognition of opaque foreign bodies in this part is thereby rendered easy.

Pharyngeal pouches, or **pressure diverticula,** arise from the posterior or postero-lateral wall of the pharynx at its junction with the œsophagus. They are demonstrated by means of an opaque bolus, some of which may enter the pouch and be there retained. By giving successive mouthfuls of opaque material it may be possible to distend the pouch, which then presents a rounded or pear-shaped opacity connected with the pharynx above (*see* Plate 89, facing p. 278, Vol. II.); opaque material subsequently swallowed is seen to pass down the œsophagus in front, or to one side, of this opacity; some degree of œsophageal delay may result from pressure of the distended pouch.

It not infrequently happens that the pouch is distended with food when the patient comes for examination, and will not afford ingress to any of the opaque material. The patient should then be re-examined on subsequent occasions, if possible immediately after the pouch has been evacuated. (Plate 58, Fig. 5)

The cervical portion of the *œsophagus* is examined with the patient in the lateral position; the thoracic portion with the patient in the right anterior oblique position, except for the lowest two inches of the gullet, the best view of which is obtained in the left anterior oblique position. These oblique positions afford an unobstructed view of the posterior mediastinum between the cardia and the vertebral column. Foreign bodies, if arrested in this part of the alimentary tract, are usually seen at the upper or lower end of the œsophagus.

The condition of the œsophageal lumen is investigated by observing the patient in the act of swallowing an emulsion of pure barium sulphate or bismuth carbonate. In the normal subject the appearances vary somewhat with the consistence of the bolus. Fluid is seen to pass down the œsophagus in a continuous stream with great rapidity as far as the cardiac sphincter. Here there is a definite delay; the sphincter relaxes at once, but only to an extent permitting of a much slower passage of the fluid into the stomach. A semi-solid bolus

passes much more slowly down the œsophagus, and there is often an appreciable hesitation opposite the upper border of the aortic arch. Definite peristalsis can be observed, but is never very vigorous in the normal subject.

Œsophageal obstruction.—This may be spasmodic or organic. **Œsophagectasis** is the name given to a spasmodic condition of the cardiac sphincter, or of the œsophagus immediately above, the exact site of the spasm being in dispute. Longstanding examples of this condition are characterized by the enormous dilatation of the œsophagus above the obstruction, this dilatation involving the lower two-thirds or even more of the canal. The lower extremity of the dilated œsophagus is seen to be cone-shaped, the apex of the cone being directed *forwards. A very thin stream of fluid may be* seen to pass from this apex into the stomach, or there may be complete obstruction lasting for considerable periods. The dilated œsophagus in these cases is generally quite inert. (Plate 59, Fig. 1.) An organic stricture can be excluded with certainty by observing the passage of a flexible rubber tube filled with mercury; this is seen to pass readily into the stomach, the weight of the mercury being sufficient to overcome the spasmodic contraction.

Organic obstruction of the œsophagus may be extrinsic, due to pressure from without, or intrinsic, due to actual stricture.

Extrinsic causes of obstruction include retropharyngeal and dorsal abscess, pharyngeal pouch, aortic aneurysm, and enlarged glands in the posterior mediastinum. When investigating a case of suspected œsophageal obstruction, examination should therefore be made of the posterior mediastinum before administration of the opaque bolus, with a view to excluding an extra-œsophageal lesion. *Obstruction due to extrinsic causes is generally much less complete than would be suggested by the symptoms.*

Intrinsic obstruction of the œsophagus may be due to fibrous stricture or to neoplasm.

Fibrous strictures result *from the healing of simple and of* syphilitic ulcers and from trauma. They may occur in any part of the œsophagus, which frequently shows considerable dilatation above the constriction. The stricture itself is commonly quite *localized*, and the œsophagus above and below the lesion is regular in *outline*

Carcinoma of the œsophagus frequently produces a *tortuous* stricture of some length. Dilatation above the obstruction is *often* absent or very slight, and vigorous peristaltic and antiperistaltic waves are commonly observed. (Plate 59, Fig. 2.) The latter may, however, occur in some cases of fibrous stricture. In very *early* carcinoma of the œsophagus the obstruction may be slight in degree, and it is then advisable to give a bolus of as solid a consistency as



FIG. 1.—Œsophagectasia



FIG. 2.—Carcinoma of œsophagus.



FIG 3—Normal stomach and duodenum

PLATE 59.

the patient can swallow. This should only be administered after the free passage of fluid has been observed, since a semi-solid bolus may cause great distress to a severely obstructed patient.

It is frequently impossible to differentiate between a fibrous stricture and one due to neoplasm.

4. THE GASTRO-INTESTINAL TRACT

The stomach and intestines are investigated by means of examination after an opaque meal. To obtain all the information possible as to the condition of the large gut, an opaque enema is also necessary. The methods adopted by different radiologists in gastro-intestinal investigations are very diverse. The following technique is that adopted by the present writer, and the interpretation of results given below holds good only when this technique is conformed to.

Twenty-four hours before the opaque meal is administered, the patient takes a dose of castor oil—½ to 1 oz. for an adult. No other medicine is given until the observations of the meal have been concluded. The patient is allowed full diet up to the morning of the examination. No breakfast is taken on that morning, but a small cup of tea and one or two slices of toast on first rising are permissible. The patient comes for the first examination at 9 A.M. or 9.30 A.M. and is given an *opaque meal* consisting of emulsion of pure barium sulphate (8 oz.), tragacanth, and water to 20 oz. Flavouring material and sugar may be added

While this is being taken, brief screen examination is made of the passage through the œsophagus and the filling of the stomach. When the meal is finished, screen examination is made in different positions of the patient, both upright and horizontal, and as many radiograms are obtained as proves necessary (*see* below).

Screen examination is reduced to the minimum, as the ultimate diagnosis is invariably made from radiograms, the writer being convinced that the screen image is utterly inadequate for the recognition or exclusion of small organic lesions of the stomach and duodenum.

The patient attends for a second examination six hours after the opaque meal. If possible, nothing is taken by the mouth between the first and second examinations, but should it appear inadvisable to enforce this abstinence, a few dry biscuits are allowed. Palpation under the screen is of importance at the second and subsequent visits, as by this means it is possible to estimate the degree of mobility of the intestinal tract, and also, by separating the superimposed coils of gut, to investigate fully the condition of all the parts seen filled One or more radiograms are obtained subsequently, to demonstrate small lesions and to confirm the screen observations.

The patient is generally seen once on the day following the meal,

and occasionally examination is necessary on the third or even the fourth day, but this is unusual.

A modification of the above technique, of value in hospital practice, consists in combining the first and second examinations at one séance at the sixth hour. For this purpose the meal is taken in the morning, but the patient is not seen until six hours later. After the sixth-hour examination has been concluded, a second meal is given for the investigation of the stomach and duodenum.

The *opaque enema* is preceded by thorough evacuation of the bowels by means of aperients and soap-and-water enemata, as many of the latter being given as necessary, and the last one preferably on the morning of the examination

The opaque enema consists of an emulsion of pure barium sulphate similar to that given as a meal, but with the omission of the flavouring material. At least three pints of this emulsion should be prepared, and should be raised to body temperature or slightly over. The enema is allowed to flow slowly into the gut through a long tube and funnel. Screen examination should be made as soon as ingress begins, and should be repeated at brief intervals until the whole of the large gut is distended. Not infrequently the enema is seen to pass into the lower ileum after the cæcum has become filled.

Radiograms are obtained at the conclusion of the examination, and also at any time during the filling of the gut that appears advisable.

The stomach.—*The method of filling, the shape, position,* tonicity, motility, and presence or absence of deformity in outline must be determined in examining the stomach; also the correct functioning of the pyloric sphincter.

In the normal stomach the first portion of the meal is seen to collect below the *magenblase* (the gas-bubble in the fundus), forming a cone-shaped opacity with the apex downwards. As more of the meal is ingested, the body of the stomach is canaliculized, and gradual expansion of the gastric walls takes place, the upper level of the meal remaining unchanged. Should the stomach already contain liquid, this appearance of canaliculization is lost, the opaque meal sinking through the stomach contents in an irregular manner and tending to collect in the most dependent portion of the viscus.

The *shape* of the normal stomach varies widely in different subjects, but falls into one of two types—(1) the cow's-horn stomach, which is disposed transversely across the abdomen, and presents no well-defined angulation between the body and the pyloric antrum; and (2) the fish-hook stomach, a much more common type, which is shaped like a letter J, the long limb lying vertically in the abdomen (Plate 59, Fig. 3).

The *position* of the normal stomach is also subject to wide variations, and, with the shape and tone (*see* below), depends on the habitus of the patient—i.e. hypersthenic, sthenic, hyposthenic, or asthenic). The cow's-horn stomach, seen in the hypersthenic subject, is confined to the upper abdomen, the greater curvature rarely reaching to the umbilicus. The fish-hook stomach, seen in subjects of sthenic and hyposthenic habitus, commonly lies very much lower in the abdomen, the greater curvature reaching two or more inches below the umbilicus, and the lesser curvature at its lowest point being ½ in. to 1 in. above that landmark.

This description applies to the stomach when the whole meal has been ingested, the expansion of the viscus by the meal naturally produces a lower position of the greater curve as filling takes place, but the position of the lesser curve is not seen to undergo any marked alteration during this process. Minor variations in position must be disregarded, but gastroptosis may be diagnosed should any part of the lesser curvature be seen below the umbilicus. The habitus of the patient must always be taken into account in considering the position (and also the shape and tone) of the stomach.

The *tonicity* of the stomach enables that organ to maintain constant the upper level of its contents, whether it be nearly empty, or distended with a full meal. In other words, in a stomach of normal tone filling takes place by equal expansion of all parts of the viscus. In the hypotonic and atonic stomach the meal tends to collect in the most dependent portion, the walls of the upper part remaining in contact.

In cases of slight defect in tone the meal may be held up in good position for a short period after ingestion, the tonic failure becoming apparent half an hour or so later. Slight hypotonus is almost invariably seen in subjects of hyposthenic habitus, and in such subjects can hardly be considered an abnormality. (Plate 60, Fig 1.)

In the hypertonic stomach the contents are seen to distend the upper part of the viscus to a greater extent than the more dependent portion, the lowest part of which is often formed by the pylorus. Hypertonus is commonly seen in the cow's-horn stomach of the normal hypersthenic subject; when present in subjects of other habitus it forms a definite abnormality.

Motility.—The muscular contractions of the stomach by means of which the food contents are mixed with the gastric secretion, and later passed through the pylorus, consist of a succession of peristaltic waves These are seen to begin quite high up on the body of the stomach, being first apparent as very slight indentations on the greater curvature. As each wave progresses downwards it becomes deeper, and when about half-way down the greater curve a correspond-

ing but smaller indentation can generally be observed on the lesser curve. Both these indentations increase in depth, that on the lesser curve somewhat the more rapidly, so that at a distance of 2 in. or so from the pylorus they have attained equality; at a slightly later stage of progress the gastric contents are almost completely divided by the constriction ring. When the wave is within ½ to 1 in. of the pyloric canal, relaxation of the sphincter usually takes place, and a small quantity of the gastric contents is driven into the duodenum, this being followed by immediate closure of the pylorus (pyloric reflex).

Peristalsis is normally seen as soon as the meal enters the stomach; the waves follow each other at fairly regular intervals and persist until the viscus is empty. Two waves, or sometimes three, can generally be seen at any one time in different parts of the gastric outline. The period which elapses after ingestion of food before the first relaxation of the pyloric sphincter depends in the normal subject on the consistency and reaction of the meal. With the liquid, neutral, opaque meal detailed above, relaxation follows almost immediately after ingestion, but does not necessarily occur in response to every peristaltic wave. Delay in the onset of peristalsis in the normal stomach may be due to nausea, faintness, or alarm.

In cases of defective motility the peristaltic waves are infrequent, irregular in time of appearance, and shallow. They frequently remain stationary for considerable periods, and tend to fade away at some distance from the pylorus. Defective motility may not be apparent for an hour or more after the meal has been taken. In hypermotility the waves start very high up on the stomach, and are increased in depth, frequency, and rate of passage to the pylorus, four or five waves being commonly observed at any one time. Hypermotility may be quite transient, or may persist until the stomach is empty.

The length of time which elapses after ingestion of the opaque meal before the stomach is empty varies widely in different normal subjects, and even in the same subject on different occasions. Two and a half hours may be regarded as the shortest normal period of emptying, and six hours as the longest, but unduly rapid emptying possesses very little significance

Disordered function of the stomach, as shown by abnormalities of tone, motility, position, and rate of emptying, bear no constant relation whatsoever to organic gastric and duodenal lesions; and the recognition of normal or abnormal function, while of the greatest importance in many instances, must not be allowed to influence in the slightest degree the diagnosis or exclusion of such organic lesions.

Organic lesions of the stomach.—The X-ray diagnosis of organic gastric lesions depends on the recognition of the deformity



Fig. 1.—Ptosis and hypotonus of stomach.



Fig. 2.—Gastric ulcer with incisura and niche.



Fig. 3.—Filling defect in pyloric antrum due to ulcer.



Fig. 4.—Pyloric stenosis (innocent).



Fig. 5.—Carcinoma of body of stomach.

PLATE 60.

in contour produced by the lesion. For this purpose serial plates are taken, the presence of an organic lesion being demonstrated by the persistence of a deformity throughout the series. Spasmodic contractions of the stomach are common; they may coexist with an organic gastric lesion, or be purely reflex phenomena, resulting from disease outside the stomach (e g. appendicular and biliary inflammations, duodenal ulcer). The two common forms of spasm are—(1) the incisura, forming a deep notch in some part of the greater curvature (spasmodic hour-glass deformity), and (2) general spasticity of the pyloric antrum, sometimes with production of a gaping pylorus.

The incisura is very commonly associated with an ulcer of the lesser curvature, while the spastic pyloric antrum is frequently seen in cases of biliary and appendicular inflammation. All forms of gastric spasm not associated with an organic gastric lesion are inhibited by administration of belladonna to *physiological effect*. Spasmodic deformities which result from lesions of the stomach itself commonly resist all medicinal attempts to attain relaxation.

Gastric ulcer.—The deformity produced by gastric ulcer may be (1) an addition to the outline of the stomach, i e. a niche (Plate 60, Fig. 2) as in penetrating ulcer, or an accessory pocket as in perforating ulcer; or (2) a defect in the gastric outline, i e. a filling defect (Plate 60, Fig 3) This deformity is an expression of the induration surrounding the crater of the ulcer.

Plates should be obtained showing the curvatures and surfaces of the stomach in profile, and in cases of difficulty the meal should be repeated after gastric lavage.

Organic hour-glass deformity of the stomach cannot be differentiated with certainty from the spasmodic form mentioned above.

Pyloric stenosis, due to simple ulcer of the stomach or duodenum, is recognized by the persistent deformity and constriction of the pyloric canal (Plate 60, Fig 4). The physiological relaxation of the pyloric sphincter, however, rarely produces a passage of more than ⅜ in. in diameter, frequently much less, and it follows that minor degrees of stenosis are exceedingly difficult to recognize radiographically, although they may be sufficiently obvious on the operating table, where a degree of pyloric relaxation is normally found far in excess of any that occurs in the ordinary circumstances of life. Pyloric spasm must be excluded by the administration of belladonna if the absence of any deformity renders the diagnosis of stenosis doubtful. It must be urged that the recognition of functional irregularities such as gastric delay, intermittent hyperperistalsis, etc., is utterly insufficient in itself to warrant a diagnosis of pyloric stricture.

Gastric carcinoma.—The basic radiographic sign of gastric carcinoma is the filling defect produced by projection of the tumour mass into the lumen of the stomach. In very early growths this defect may be so small as to escape recognition even in the most careful examination. In a slightly later stage the defect may be clearly demonstrated, but differentiation from simple ulcer may be impossible.

Generally, however, these cases do not come for X-ray examination until the growth is of sufficient size to produce large irregular defects in the gastric contour (Plate 60, Fig. 5). Pyloric carcinoma, in its earlier stages, produces an annular defect in the pyloric antrum, not infrequently associated with a gaping pylorus due to infiltration of the pyloric sphincter (*Plate 61, Fig. 1*). In the later stages of this growth pyloric stenosis becomes evident. A valuable confirmatory sign in gastric carcinoma is the complete absence of peristalsis over the affected area.

The filling defect of gastric cancer may be simulated more or less closely (1) by pressure on the stomach from without, by the vertebral column, extragastric tumours, or a dilated colon: changes in posture will usually produce a disappearance or alteration in such defects; (2) by the presence of food in the stomach when the opaque meal is taken: should this be suspected, re-examination must be made after proper preparation.

Carcinoma occasionally produces an hour-glass deformity, but the defect involves both lesser and greater curves; while in the hour-glass stomach due to simple ulcer the defect is confined entirely, or almost so, to the greater curve.

In scirrhous carcinoma the stomach presents the appearance of a narrow, rigid tube through which the meal passes with great rapidity, the pylorus being widely and permanently gaping.

Benign gastric growths, and inflammatory tumour formations, such as tuberculosis, cannot generally be differentiated with any degree of confidence from carcinoma.

The duodenum.—The chyme which leaves the stomach at each relaxation of the pyloric sphincter spreads out in the first part of the duodenum to form the "duodenal cap" (Plate 59, Fig. 3). This presents a dense cone-shaped opacity, with perfectly smooth and regular sides, the flat base of the cone resting on the duodenal surface of the pyloric sphincter. The duodenal cap persists unaltered for an appreciable time, and is then subjected to a contraction which forces the duodenal contents onwards. The chyme is always much more finely divided after it leaves the first part of the duodenum, and remains in this stage until it reaches the lower ileum. The passage through the second and third parts of the duodenum is pro-



Fig 1—Small annular pyloric carcinoma



Fig 2—Small duodenal ulcer



Fig 3—Duodenal ileus

PLATE 61.

duced by vigorous peristaltic waves, each wave passing over a short segment of gut only. At two points a definite arrest in the onward passage is commonly seen—(1) just below the papilla of Vater, (2) half-way along the transverse portion of the duodenum. These temporary arrests are associated with to-and-fro movements of the chyme. The appearances are best seen when the meal is leaving the stomach with considerable rapidity; they represent the normal passage of the meal through the duodenum in these circumstances. They presumably constitute the picture which has been labelled "writhing duodenum," and have been erroneously ascribed to duodenal obstruction; true duodenal obstruction presents an entirely different radiographic picture (*see* below).

Duodenal ulcer nearly always affects the first part of the duodenum. The radiographic diagnosis depends on the demonstration of a persistent deformity of the duodenal cap This deformity can only be shown in a series of radiograms in which the cap is seen fully formed. Every effort must be made to secure a normal picture of the duodenal cap, and one such normal picture excludes the presence of an ulcer, in spite of apparent abnormalities in other radiograms. In other words, the diagnosis of ulcer is only made when the radiologist is satisfied that the duodenal cap is never normal The deformity produced by an ulcer may be entirely organic, or partly organic and partly spasmodic; it commonly takes the form of a defect in the outline of the cap, but occasionally a projection is seen, due to the filling of the crater of a perforating ulcer. The degree of deformity bears no constant relation to the size of the ulcer, owing to the frequent presence of spasm. Plate 61, Fig. 2, shows considerable deformity of the cap, but the crater of the ulcer measured $\frac{1}{10}$ in. in diameter, and the lesion was only demonstrated clinically by inspection of the mucosa after opening the duodenum. It is generally impossible to state whether a duodenal ulcer is active or has healed.

Periduodenal adhesions may closely simulate ulceration, and the differential diagnosis may be impossible. The deformity produced by adhesions may, however, become less in degree as the stomach empties, while in ulceration the deformity undergoes no diminution.

Duodenal diverticula are not very uncommon. They present rounded or branched extraduodenal opacities, generally lying internal to the first or second parts of the duodenum. They are frequently multiple, and of considerable size.

Duodenal ileus.—This obstruction of the duodenum arises at the point where the superior mesenteric vessels cross the gut. It is sometimes seen after the operation of gastro-jejunostomy, but apart from this it may occur in patients who present severe degrees of

enteroptosis. The X-ray appearances are very striking and characteristic. The duodenum proximal to the obstruction rapidly fills up with the opaque chyme, and is then seen to be greatly dilated. An occasional peristaltic wave may be observed, but muscular contractions are generally conspicuous by their absence, the dilated gut being quite inert. At the site of the obstruction the gut can be quite plainly seen to be flattened in an antero-posterior direction (Plate 61, Fig. 3). Opaque material may remain in the dilated duodenum for a considerable time after the stomach is empty.

Obstruction at the duodeno-jejunal junction is an occurrence of extreme rarity, and is invariably the result of a gross organic lesion, e g pressure of a renal tumour.

Jejunum and ileum.—The passage of the meal through these portions of the intestinal tract is effected by means of frequent peristaltic waves, having no fixed points of origin or cessation, and generally each extending over a comparatively short segment of gut. In addition to this peristalsis, the gut undergoes frequent segmental division by means of isolated constrictions. In this way a certain amount of to-and-fro movement is conveyed to the intestinal contents. The movements of the small gut are best studied in the jejunum, where the chyme is finely divided and the individual coils can be readily separated. In the lower ileum the muscular contractions are much less obvious.

The terminal ½–1 in. of the ileum often presents a pronounced spasmodic constriction which is apparently physiological; it has been described as the "ileal sphincter." The length of time taken by the passage of the chyme from the pylorus to the terminal ileum is 2–3½ hours. There is frequently a delay of ½–1 hour after the terminal ileum is filled before entry into the cæcum begins.

Involvement in adhesions may be demonstrated by fixation of coils of gut in the abdomen or to one another. It is frequently impossible to determine the mobility of the lower ileum, when this is prolapsed deeply in the pelvis.

Adhesions may give rise to definite evidence of obstruction of a coil of small gut, the lumen of the gut behind the obstruction being distended with opaque material for a considerable time. Small-gut obstruction is, however, rarely so severe as to produce any very great delay in the passage of the liquid contents.

Ileal delay is almost invariably a result of neuro-muscular derangement (*see* p. 695).

The **large bowel** may be examined by means of the opaque meal, and also the opaque enema. The latter method should never be omitted in cases of suspected organic disease of the large gut.

The passage of the contents through this portion of the alimentary

tract is effected by means of occasional contractions of the circular muscle, occurring simultaneously over a considerable segment of gut, and accompanied by muscular relaxation distal to the contracted segment.

The contractions produce extensive progressions of the intestinal contents, known as "mass movement." The contractions occur at infrequent intervals, possibly only three or four times in the twenty-four hours, and each contraction lasts for a few seconds only; hence it is obvious that opportunities of studying this phenomenon are limited.

Small isolated muscular contractions probably occur continuously in the large gut, but are not associated with progression of the contents, and cannot be recognized radiographically.

The rate of passage of the large-gut contents is subject to the greatest variation in different normal individuals, and in the same individual on different occasions.

Commonly the head of the opaque column is seen at the hepatic flexure within eight hours of the ingestion of the meal, at the splenic flexure within twelve hours, and in the pelvic colon in twenty-four hours. These figures are merely approximate, and no importance whatever attaches to any but very great divergences from this standard. It must be remembered that the opaque material in the large gut mixes with the residue of meals taken before, and—especially—after, the opaque meal. Hence the rate of progress is taken from the head of the opaque column, and small residues remaining in the proximal part of the large gut are disregarded.

The *position* of the large gut is greatly influenced by the habitus of the patient. In the sthenic or slightly hyposthenic subject the hepatic flexure commonly lies 1–1½ in. above the iliac crest when the patient is upright; the splenic flexure being 2–3 in higher. The transverse colon varies in length, but generally descends to within 1 or 2 in. of the symphysis pubis. There can be no doubt that a very low position of the large gut is not in itself a cause of disability. Such positions are found in quite a large proportion of perfectly healthy subjects throughout adult life. It is only when the natural support of the intra-abdominal organs (i.e. the intra-abdominal pressure) has failed, with resulting traction on the peritoneal attachments and their contained vessels and nerves, that the varied symptoms referred to enteroptosis are exhibited.

Operative attempts to fix the gut at a higher level are seen to be followed by a gradual return of the prolapse, unless successful postoperative measures have been adopted to restore the normal intra-abdominal pressure. There is, moreover, abundant evidence that a low position of the large gut has not *per se*, any causal relation-

ship with delay in the passage of the intestinal contents. When the two conditions are associated, the delay is commonly due to general neuro-muscular defect involving striped and unstriped muscle, and the ptosis of the colon is merely a manifestation of the inefficiency of the abdominal wall.

Neoplasms of the large bowel are best demonstrated by means of the opaque enema, and are recognized as constant filling defects in the lumen of the gut. Benign growths, e.g. polypi, rarely provide any radiographic evidence of their presence. Carcinoma, on the other hand, except in the very early stages, is apparent as a definite filling defect producing some degree of constriction of the lumen. Complete obstruction to the passage of the enema is rare, unless impacted fæcal masses are present above the growth.

Diverticulitis.—Both the meal and the enema should be employed in attempting to demonstrate this condition. The radiographic appearances of intestinal diverticula consist of one or more rounded extramural opacities. Care must be taken to assure that these opacities are in fact extramural, and do not merely represent the contents of a saccule temporarily isolated from the main lumen (Plate 62, Fig. 1). Persistence of the opacities after evacuation of the remainder of the opaque material is the most conclusive sign of true diverticula. Diverticulitis is commonly associated with some degree of *stricture of the gut; the stricture is frequently long and tortuous, but the recognition of diverticula is necessary for the exclusion of neoplasm.* The occasional coexistence of carcinoma with diverticula must be remembered.

Other inflammatory conditions of the large gut, unless associated with stricture, do not generally provide any radiographic data for diagnosis. Persistent absence of sacculation is, however, sometimes seen *in longstanding cases of chronic colitis.* Fibrous stricture, resulting from old benign ulceration, cannot be differentiated from neoplasm by radiographic means alone.

The vermiform appendix.—Definite information as to the condition of this structure can only be obtained by direct observation, or, in other words, if the opaque *contents of the cæcum pass into* the appendix. With the technique here adopted the appendix is seen filled at some time during the examination in a large proportion of cases. Frequent examinations must be made, palpation under the screen being confirmed by radiograms; the latter will frequently demonstrate an appendix which is invisible on fluoroscopy, *and will* always supply detailed information which cannot be gathered from the screen image. *The appendix* commonly fills about the sixth or eighth hour after the meal, but may not be seen until the twenty-fourth-hour examination. When once demonstrated, examinations



Fig. 1.—Colic diverticula.



Fig 2—Chronic appendicitis



Fig 3—Biliary calculi and duodenal ulcer.



Fig 4—Renal calculus.



Fig. 5—Renal calculus.

PLATE 62.

should be repeated at intervals until the lumen is empty of opaque material. This commonly coincides in normal subjects with the emptying of the cæcum. The normal appendix is seen to be—(1) freely mobile in the abdominal cavity and from adjacent structures, (2) regular in lumen, (3) free from acute, permanent kinks, (4) not tender on direct pressure. Abnormality can be inferred from defect in any of these qualities, and also if prolonged retention of contents is observed. Retention for as long as three weeks has been observed in a chronically inflamed appendix (Plate 62, Fig 2).

Intestinal stasis.—Without in any way minimizing the importance of intestinal stasis, it must be pointed out that many descriptions of this condition appear to be based on a completely erroneous view of the normal rate of passage of the intestinal contents and a failure to recognize the wide variations which exist in normal subjects, and in the same subjects at different times. There can be no doubt that intestinal toxæmia depends primarily on intestinal infection, and is very frequently unassociated with any delay in the passage of the bowel contents, at any rate until a very late stage, when the inflammatory process has damaged the neuro-muscular apparatus.

The diagnosis of intestinal stasis is, in point of fact, beset with difficulties and possibilities of error, and every case should receive most careful individual consideration.

Very briefly, the maximum emptying time of the normal stomach may be taken as six hours; this only holds good if the patient is up and about, and provided that no food is taken during the emptying process. The terminal ileum will then be found filled within 3½ hours of ingestion of the opaque meal, and the cæcum commences to fill ½-1 hour later. The ileum should be free of opaque material 4-4½ hours after the stomach is empty. When gastric delay is present it will be impossible to starve the patient until the stomach is empty, and the food taken will then mix with the opaque residue, and produce a spurious increase in gastric delay, and consequent increase in delay in emptying of the ileum. It is therefore advisable to adopt as the criterion of ileal delay the time at which the head of the opaque column enters the cæcum. If, with the stomach empty, or nearly empty, the cæcum has not begun to fill at the sixth hour, definite ileal delay is present.

Delay in the large gut presents an even more difficult problem; it has been stated that the entire meal should be evacuated in seventy-two hours, and this appears to be a reasonable estimate. Small residues in the proximal colon at the end of twenty-four hours may be disregarded, provided that the head of the column has reached the pelvic colon. Any considerable residue in the proximal colon persisting to forty-eight hours indicates definite retention in that

part. The most common site of delay is at the pelvi-rectal junction, the passage of the contents to this point being accomplished without abnormality.

Delay also sometimes occurs as a result of defective defæcation, fæcal matter remaining in the rectum after the bowels have acted.

Delay in the passage of the intestinal contents, in the absence of gross mechanical obstruction, is invariably due to neuro-muscular defect, the causation of which can rarely be demonstrated. Chronic *inflammatory lesions involving the bowel*, such as chronic appendicitis, or pelvic peritonitis, are sometimes associated with delay, but no constant effect is observed in such cases. Examination before and after such operations as colopexy, undoing of "kinks," etc., demonstrates that the operative procedure has had no influence whatever on the rate of passage of the meal; and the same statement holds good in many cases of appendicectomy, even where very definite inflammatory changes have been found in the appendix.

The biliary tract.—Biliary *calculi* can be demonstrated by X-ray examination in a small percentage of cases only. When seen they commonly present a typical "ring" opacity, due to deposition of opaque calcium salts upon the translucent cholesterin calculus (Plate 62, Fig. 3). Occasionally, owing to excessive deposition of opaque salts, the calculus presents a more uniform opacity, and may be mistaken for a renal calculus. An attempt must then be made to show the opacity outside the shadow of the kidney outline. A lateral view is conclusive, provided the opacity can be seen in this position. Examination of the stomach and duodenum is often of service in providing confirmatory evidence of a biliary lesion; the stomach frequently presents a marked spasticity of the pyloric antrum, relaxing under sufficient doses of belladonna, and the duodenum may show deformity suggestive of periduodenal adhesions

VII. THE URINARY TRACT

In investigating the urinary tract the technique adopted is of supreme importance. The patient should be carefully prepared by means of mild aperients repeated on several nights before the examination. He should come to the radiologist without breakfast, and should have taken as little food as possible on the day preceding the examination. In all cases the whole urinary tract should be included in the examination. Two plates are sufficient for this purpose: the first includes the lower ureters and bladder, the tube being centred under the symphysis pubis and the plate resting on the abdomen; the second plate includes the upper ureters and kidneys. It is placed on the back, the patient lying prone on the couch with a pad of wool

below the epigastrium, and the tube is centred over the second lumbar spinous process.

It is absolutely essential to ensure that the position of the patient and the centring of the tube be accurate, as in this way only can the normal position of the ureters in relation to the vertebræ and pelvic bones be predicated with certainty.

Radiograms must be of good quality, free from the shadows of intestinal gas and of fæcal matter. A satisfactory radiogram of the upper part of the urinary tract should show—

(1) The transverse processes of the lumbar vertebræ
(2) The outer borders of the psoas muscles.
(3) The 11th and 12th ribs.
(4) The posterior portions of the iliac crests.
(5) The outlines of the kidneys.

The two sides should be absolutely symmetrical.

Enlargement of the kidney, if of moderate proportions, can be recognized from the enlarged outline. Great renal enlargement renders the whole loin opaque, and obliterates the margin of the psoas. The outline of the kidney in these cases is often imperfectly seen.

Tuberculosis of the kidney may present no radiographic evidence. In other cases enlargement of one or both kidneys may be seen, the nature of the enlargement not being demonstrated. Sometimes, however, the deposition of calcium salts in caseous material produces an appearance typical of tuberculosis, the enlarged kidney showing multiple ill-defined opacities, irregular in density and outline. The differentiation from renal calculus in these cases is generally easy.

Urinary calculi (Plate 62, Figs. 4, 5).—The calculi which form in the urinary tract produce a definite opacity in a radiogram of good quality, with the exception of the pure uric-acid calculus, which is, for practical purposes, non-opaque to X-radiation; this calculus is not uncommon in the kidney in boys, and in the bladder of old men.

The opacity of urinary calculus is generally of uniform density throughout its extent. Sometimes the density is greatest over the central portion of the opacity, and fades off towards the margins, but this diminution is gradual and regular. Large vesical calculi sometimes produce definitely laminated opacities.

The opacity may be of any shape, but certain forms of outline are very common and characteristic—e.g. triangular, dumb-bell-shaped, and branched opacities in the region of the renal pelvis, rounded and fusiform opacities in the line of the ureter (Plate 63, Fig. 1), rounded and oval opacities in the bladder region.

The position of the opacity in relation to that occupied by the renal structures on the radiogram is of paramount importance. The

normal line of the ureter in a radiogram taken antero-posteriorly is from the apex of the transverse process of the 2nd lumbar vertebra, just across the tip of the 3rd lumbar transverse process, thence to the sacro-iliac synchondrosis, thence to just internal to the spine of the ischium; it then curves inwards across the floor of the pelvis to the bladder. Anatomical abnormalities of the ureters and renal pelvis, though rare, must not be forgotten; in cases of doubt the passage of an opaque ureteric catheter, or the injection of an opaque salt into the renal pelvis, will place the position of the renal organs beyond dispute (*see* below).

The opacities of urinary calculi must be distinguished from—

(1) Caseous material in the kidney.
(2) Intestinal contents.
(3) Calcareous glands.
(4) Biliary calculi.
(5) Calcified appendicular concretions.
(6) Phleboliths.

Caseous material commonly produces an ill-defined diffuse opacity, showing irregular variations in density throughout its extent.

Intestinal contents must be excluded by further preparation. The opacities produced are generally faint and ill-defined.

Calcareous glands may cause great difficulty in diagnosis, which can, however, generally be overcome by attention to the following points: (*a*) Calcified abdominal glands are frequently multiple; (*b*) they are mobile, so that it is impossible to displace the opacities outside the area occupied by the urinary organs; and (*c*) the opacity of calcareous glands is generally very irregular in density and outline—often, in fact, definitely punctate.

For *biliary calculi*, *see* p. 696.

Calcified appendicular concretions are usually fusiform in shape but the long axis of the opacity rarely corresponds to the line of the ureter. The recognition of calcified ileo-colic glands, frequently present in chronic appendicular inflammations, will be of assistance in pointing to the nature of the lesion.

Phleboliths are common in the pelvic veins. They produce small round opacities, frequently multiple, lying immediately above the pelvic brim or overshadowed by the body of the pubis. The position of the opacities renders the diagnosis clear.

Prostatic and urethral calculi.—Calculi in the prostatic urethra produce opacities which lie behind the symphysis pubis.

Prostatic calculi are usually small, multiple, and irregular in outline. They are overshadowed by the bodies of the pubic bones.

Pyelo-radiography.—Injection of an opaque salt, such as potassium bromide or collargol, into the pelvis of the kidney provides



Fig. 1.—Ureteric calculus



Fig. 2.—Normal pyelogram: a biliary calculus lies external to the renal pelvis.



Fig. 3.—Dilated renal pelvis



Fig. 4.—Vesical diverticula

PLATE 63.



Fig 1.—Pneumoperitoneum: normal liver and kidney.



Fig 2.—Pneumoperitoneum: enlarged spleen.

PLATE 64.

useful information as to the size, shape, and position of that structure. (Plate 63, Fig. 2.) Not only can the relations of the ureter and renal pelvis to a doubtful opacity be thus demonstrated, but dilatations and malformations can also be well seen. Dilatation may affect the renal pelvis chiefly, or may be most marked in the calyces, and these two types can be differentiated (Plate 63, Fig. 3).

Vesical diverticula can be demonstrated by the injection of an opaque solution into the bladder (Plate 63, Fig. 4).

VIII. EXAMINATION OF THE SOLID ABDOMINAL VISCERA

With the exception of the kidneys, and occasionally the spleen, radiography ordinarily provides no information as to the condition of the solid abdominal organs, the abdomen presenting a uniform opacity.

The introduction of oxygen through a hollow needle into the peritoneal cavity completely alters this state of affairs by separating the intra-abdominal structures, and surrounding them to a greater or less extent with a medium exceedingly translucent to X-radiation. (Plate 64, Figs. 1, 2; Plate 65, Figs. 1, 2.)

The technique for the production of this pneumoperitoneum is very simple, but the method is not wholly free from danger.[1] The radiographic examination must be carefully planned to ensure that the organs to be observed are enveloped to the maximum possible extent in oxygen. At the conclusion of the examination the needle is reinserted, and the oxygen allowed to escape; or the gas may be left to absorb. In either case the patient should remain in bed for at least twenty-four hours, at the end of which time most of the gas will have been absorbed. Radiography after production of pneumoperitoneum is of value—

(1) In all diseases associated with alterations in the contour or size of the solid abdominal organs.

(2) In demonstrating the presence of adhesions of the solid viscera and of the intestines to the abdominal parietes.

(3) In investigating abdominal tumours.

(4) In cases of urinary calculus where ordinary radiography is inconclusive.

[1] In a recent case the Editor has seen a fatal acute pneumothorax result *from* the passage of oxygen, introduced suprapubically, through a congenital defect in the diaphragm, whose presence could not have been detected beforehand. Other accidents have been recorded by Josefson (*Hygeia*, 1922, xxxiv. 1) and others, and have included surgical emphysema, injury to intestine, puncture of veins with subsequent gas-embolism, and sudden heart-failure.

The present writer has not been successful in demonstrating biliary calculi by this method, although an enlarged gall-bladder can be well seen.

Ventriculography.—The introduction of oxygen into the cerebral ventricles prior to radiography has been practised in the United States as a means of investigating the location of cerebral tumours. The method has not been adopted in this country, and is not, apparently, free from danger.

Jacobæus has also injected oxygen into the spinal theca for the purpose of localizing exactly the position of a spinal tumour; and the block, by the pressing tumour, to the passage of the oxygen up the theca is demonstrable by radiography.



Fig 1—Pneumoperitoneum: normal kidney



Fig 2—Pneumoperitoneum pelvic organs.
B, Bladder, U, uterus; B L, broad ligament R O, right ovary, L.O, left ovary; G, calcified gland

PLATE 65.

GENERAL ANÆSTHESIA

By J. BLOMFIELD, O.B.E., M.D.

The scope of this article does not allow any consideration of the purely physiological or chemical aspects of general anæsthesia A general knowledge of these on the reader's part is therefore assumed, and the subject is dealt with from a solely practical point of view.

PRELIMINARY STEPS

Certain steps should be taken in all cases before the administration of a general anæsthetic. Thus, a brief examination of the circulatory and respiratory efficiency of the patient should be made by careful palpation of the pulse, and by placing a hand upon each side of the chest while a deep breath is drawn. The inside of the mouth is then inspected to ensure the absence of artificial teeth or other foreign

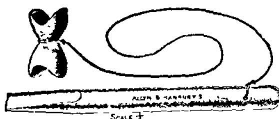


Fig. 172.—Wooden prop and wedge.

bodies, and also to note the shape of the palate and jaws and the coaptation of the teeth. Nasal inefficiency and inconvenient locking of the teeth during spasm will be guarded against by the insertion of a small prop between the teeth before beginning the administration (Fig. 172). The anæsthetist should also be provided with a small wedge (Fig. 172), a Mason's gag (Fig. 173), and a pair of tongue forceps. The condition of the patient's urine should be ascertained, although this precaution is not necessary before the administration of nitrous-oxide. It is also advisable to find out whether an anæsthetic has been previously taken, as useful knowledge may be gained of any peculiarity of behaviour on the patient's part during the former administration.

The best position for the patient, unless specially contra-indicated, is lying upon his back, with the head slightly raised above the level of the shoulders and turned to one side. Clothing, if worn, must be quite loose round the neck, waist, and chest. Strict quiet should be maintained by all present, and no moving of instruments or other source of noise be allowed to disturb or alarm the semiconscious patient on his passage to full anæsthesia. The sense of hearing lasts long, and is accentuated before unconsciousness supervenes. Moreover, it is important not to cut bandages, etc., or to move the cover-

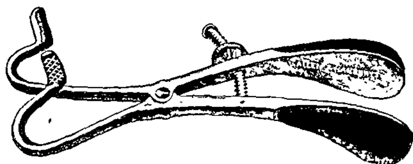


Fig. 173.—Mason's gag.

ings of a partially anæsthetized patient, to whom such proceedings would suggest the premature beginning of the operation and might cause the shock of alarm.

SIGNS OF ANÆSTHESIA

Three cardinal symptoms should be present before anæsthesia is accepted as sufficiently deep for operating purposes. These are: (1) relaxation of muscles, as proved by the limpness with which a limb falls if raised and then released; (2) absence of conjunctival reflex, and diminution of corneal reflex, shown by the faint response of the lids when a finger is lightly drawn over the pupil of the eye (this test is seldom necessary, or advisable); (3) stertorous breathing, recognized by the sound made in respiration if the patient's chin is depressed or allowed to drop.

In the case of very robust subjects, or those in whom an operation is to be performed on a particularly sensitive part of the body or within the abdomen, anæsthesia should be carried slightly farther than this before the surgeon commences. That is to say, the corneal reflex should be quite abolished. The pupil, after being enlarged in the early stages of induction, is, when proper surgical anæsthesia is reached, about half-way between full dilatation and extreme contraction in size, and reacts to light. It is slightly larger in ether than in chloroform anæsthesia, where safety is best preserved by keeping the pupil small.

The size of the pupil, however, as an indication of the depth of anæsthesia is not trustworthy during the early stages of an operation. Peripheral impressions cause variations in the pupil. When opium or allied drugs have been given beforehand, the value of the size of the pupil as a guide to the depth of narcosis is discounted. The pupil remains small after a hypodermic of morphia gr. ¼, however deep the narcosis, in most persons. Even ⅛ gr. contracts the pupil in many instances, and keeps it contracted against the dilating effect of deep ether or chloroform narcosis. In all cases the anæsthetist should be guided mainly by the **respirations.** Every breath should be either heard or felt; for while breathing is regular and at least as vigorous as that of normal sleep, trouble due to the anæsthetic need not be feared. At the same time a close watch should be kept upon the **colour**, as estimated by observation of the lobe of the ear. The **pulse** should be felt from time to time, and the condition of the conjunctival reflex ascertained every few minutes, to confirm the information gained by watching the breathing and the colour.

In the case of operations under ether, chloroform, and similar anæsthetics, it is important to realize that, when once anæsthesia is induced, comparatively small amounts of anæsthetic are required to maintain it. Thus, in long operations a constantly diminishing amount of the drug is applied, so that in the case of chloroform, for instance, a vapour as weak as ½ per cent. constantly supplied often suffices to maintain anæsthesia during the greater part of the operation. It is important not to mistake movements of limbs or digits due to an **anoxæmic condition** of the blood for the movements of light narcosis. These movements, sometimes of a twitching, sometimes of a rhythmical character, call for less anæsthetic and more air—not for more anæsthetic.

SELECTION OF THE ANÆSTHETIC

When a general anæsthetic is required, the first consideration is the choice of the most suitable drug to employ in the particular case. We will therefore first consider the selection of the anæsthetic. Here we are at once confronted with the difficulty of laying down rules equally applicable to the expert and to the inexpert. In the case of the **inexpert administrator** the wisest plan is undoubtedly to select for all cases the same routine anæsthetic, as far as this is possible, so that in the administration of that one, at any rate, the practitioner may become experienced. For this purpose we require (1) an anæsthetic of wide applicability, (2) one the administration of which can be conducted with simple and portable apparatus, (3) one that is not easily rendered dangerous, and (4) one the administration of which is easily learnt.

To meet these requirements there is nothing better than the mixture of chloroform and ether known as the C.E. mixture[1] administered from a drop-bottle upon an open mask. The drop-bottle should hold at least three ounces, and should be capable of administering the drops slowly, rapidly, or in a continuous stream. This is possible from a bottle provided with a top designed by Hewitt (Fig. 174) or from Thomas's drop-bottle. The mask should be a light metal frame enclosing an area of about five inches by three, and high enough to avoid touching the nose when applied to the patient's face. It should be covered with a single layer of thin flannel or domette. The most convenient form of mask is Schimmelbusch's (Fig. 175), having the handle placed at one side. The flannel or domett should be cut so as to leave a margin beyond the metal edge of the mask, and should be fresh for each case. As the material is inexpensive and requires no elaborate fitting or stitching, this change is easily effected.

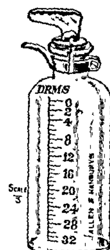


Fig. 174. Hewitt's drop-bottle.

Method of administration.—The mask is applied closely to the face, and after a few breaths the mixture is added, a very few drops

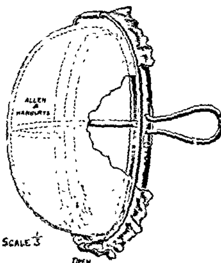


Fig. 175.—Schimmelbusch's mask.

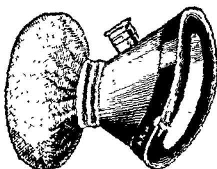


Fig. 176.—Ormsby's ether inhaler.

at a time. During the first two minutes the mixture is poured on in such small quantities that never more than one-quarter of

[1] The mixture is made of chloroform 2 parts and ether 3 parts, by volume, shaken together. It must be freshly made.

the surface of the mask is moist. Then it is added more freely until in the case of men the whole surface of the mask (in the case of women three-quarters, and in the case of children one-half of the surface) is kept moist with the liquid. At least *four minutes* should elapse between the beginning of the administration and the moment when the maximum quantity is first placed upon the mask. When anæsthetizing very robust or alcoholic subjects, it is advisable to have at hand an Ormsby's inhaler (Fig. 176) and an ounce of pure ether. If the stage of excitement becomes unduly marked, as may be the case with these difficult subjects, it is quickly quelled and anæsthesia established by pouring the ether on to the sponge of the inhaler and applying the face-piece closely to the patient's face. This procedure, however, should not be adopted till the mixture has been in use for at least four or five minutes. When stertor arises, as will quickly occur, the inhaler is removed, and anæsthesia continued by use of the open mask and C.E. mixture. The average induction period with this method is eight minutes. During operation the mixture is used at the rate of about one ounce in fourteen minutes.

Some rigidity of the jaw muscles and of the limbs, with attempts to sit up, is not uncommon during the induction stage. This is met by continuing the administration smoothly, without any attempt to "rush" the patient by greatly increased dosage. Nor should strenuous efforts be made to keep the patient perfectly still; it is better to allow him free movement within limits—care being taken, of course, that he does not hurt himself or those near him, and that he does not in his inco-ordinate and semi-conscious movements lurch himself off the operating table. The most powerful subjects can be kept in a state of perfect anæsthesia for long periods by this method, and, on the other hand, it may be safely used in the case of infants or of the most feeble. In the latter instances care is required not to overdose; only a small portion of the mask's surface should be allowed to be moist with the mixture.

Turning now to the choice of anæsthetic for a more **expert administrator** who is not confined to a routine measure, we must take into consideration—(1) the safety of the patient; (2) the convenience of the operator, which involves the consideration of the kind of anæsthesia available with each particular anæsthetic, and its suitability to the requirements of the case in question. Thus, **nitrous-oxide with oxygen or air** is the safest anæsthetic at our disposal, yet the fact that it cannot always be relied on to produce muscular relaxation or perfect stillness when sensitive parts are handled limits its applicability. This limitation is emphasized by the cumbrous nature of the apparatus. The most recent forms of

apparatus—those, for example, of Marshall and of Shipway—have largely surmounted this difficulty. By the use of these instruments, and in hospital work by the use of Boyle's apparatus (Fig. 177), a great many operations can be performed under the anæsthesia of continuous nitrous-oxide and oxygen. For many more the gases do not suffice unless reinforced by ether or C.E. mixture, which can be easily supplied along with the gases by all the apparatus mentioned. To get the best results from nitrous-oxide and oxygen in *major surgery* much practice is needed. Preliminary hypodermic injection of narcotics is always necessary. The gases are not to be regarded as *so absolutely safe for long operations* as for minor procedures. Removal of teeth, or of small tumours or sebaceous cysts, opening of abscesses, amputation of fingers, and dressings of a painful character are common occasions when nitrous-oxide is most suitably employed. Nitrous-oxide and oxygen are best applied to long operations on comparatively insensitive parts, e.g. bones.

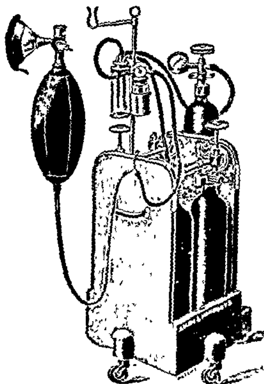


Fig. 177.—Boyle's nitrous-oxide and oxygen-and-ether apparatus.

Nitrous-oxide is not a safe anæsthetic in cases where there is dyspnœa. Mechanical narrowing of the air-passages—e.g. cellulitis of the neck with œdema of the glottis—emphatically contra-indicates the use of "gas" or any anæsthetic *that is not given on an open mask along with free supply of air.*

Next to nitrous-oxide in point of safety comes ether, which should be chosen for the majority of cases which are not met by the former anæsthetic. Ether is to be avoided, however, for all cases where there is an acute affection of the air-passages—e g. diphtheria, acute bronchitis, and active phthisis. In active phthisis *chloroform* should be employed.

The cases in which ethyl-chloride is *of special advantage* are

those in which nitrous-oxide is not suitable but the time required is short. Thus, small children who are to have tonsils and adenoids removed, abscesses opened, etc., provide a field in which this drug is of great use, particularly in hospital practice, where time is a pressing question. Nervous people, who are anxious to become unconscious quickly, are also subjects with whom ethyl-chloride may be employed with special benefit.

Although *valvular disease of the heart* does not *per se* necessitate any departure from the ordinary rules in choosing an anæsthetic, unless compensation is broken, yet whenever the heart's action is weak ether has special advantages. Thus, in cases of collapse from recent injury or long, grave illness, this is the drug to employ, generally by the "open method." Even in cases of *empyema*, which are usually best met by chloroform, if the general condition is sufficiently feeble, "open ether" should be employed; and the same may be said of *asthmatic subjects.*

In cases of *renal disease* with marked albuminuria, chloroform is less likely to increase the albumin than is ether. Moreover, cases of œdema of the lung have occurred with the latter drug in these circumstances. *Diabetes* may be terminated by coma after anæsthesia, however induced. The danger is diminished by reducing the sugar beforehand, and by shortening the anæsthesia as far as possible. Persons under the influence of *opium* or similar drugs require particularly careful handling during anæsthesia, from the point of view of giving only as much of the anæsthetic as is absolutely necessary. Those accustomed to the free use of *alcohol* require large amounts of anæs thetic. Ether should play a prominent part in the management of these cases, in which there is frequently present a fatty condition of the heart that is not compatible with safety if chloroform is freely employed.

Patients suffering from *conditions associated with drowsiness*—e.g. cerebral tumour, advanced renal disease—require but little anæsthetic. Generally in such cases a deep degree of anæsthesia is only necessary to ensure quiet during the skin incision, as, for example, while the flap is made from the scalp in cerebral cases and during the first incision in the loin in calculus cases in which uræmia has already begun. During all the subsequent stages of the operation the anæsthetic is administered in the smallest possible quantities. Chloroform is generally best suited to these cases. *Pregnancy* is no bar to anæsthesia if operation becomes necessary during this condition. Care must be taken, though, to avoid the causation of cyanosis, which may induce premature labour. In *childbirth* itself chloroform is well borne, and in ordinary cases is used only during the pains and after the os is nearly fully dilated. A condition of surgical anæsthesia is not

required. When this is necessary for operative midwifery, safety is best ensured by using ether, as in surgical cases. The process known as "twilight sleep" is much favoured for labour by some authorities. The *injection* of morphia gr. $\frac{1}{6}$ and scopolamine gr. $\frac{1}{150}$ is given to primiparæ as soon as the pains are coming regularly every few minutes and are causing distress. To multiparæ the injection is given directly labour begins. Further injections of gr. $\frac{1}{400}$ scopolamine are given when found necessary by the memory test (showing the patient a common object, and after half an hour trying whether she remembers having it shown to her). Thorough conduct of "twilight sleep" requires almost *constant attendance* of the anæsthetist during *many hours*. *Lactation* has no especial bearing upon the choice of anæsthetics, but it is important that the baby be *not suckled until* the mother has eliminated the *anæsthetic*. Thus it *is best to* have the baby *bottle-fed for* twenty-four *hours after* the mother's *operation. In this* connexion *it may* be mentioned that when the *mother is subjected to* a long *administration of* chloroform during *child*birth the baby *may* be drowsy with the *drug* when born, and *may require extra* stimulation to ensure proper breathing.

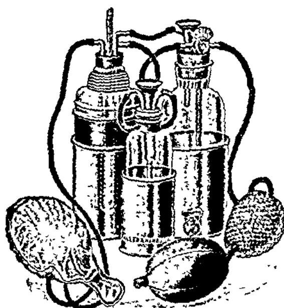


Fig. 178.—*Shipway's* warm-vapour apparatus.

Nature and the site of operation as bearing upon the choice of anæsthetic.—*Operations upon the head, neck, face, and pharynx,* when they can be done within about *ten minutes*, are best met by producing a deep ether anæsthesia and then removing the apparatus, *giving* no more anæsthetic while the operation is performed. Most cases of sebaceous cyst, harelip, epulis, epithelioma of lip, and *suppurating glands of* neck are well managed in this way. When a *long operation* is necessary the anæsthesia *thus produced* is allowed *to become lighter until* a brisk corneal reflex has returned, and then *chloroform is administered* from a Junker's inhaler and tube (Fig. 187). If it is desired to avoid chloroform, anæsthesia can be

kept up by pumping into the mouth warm ether vapour by means of Shipway's warm-vapour apparatus (Fig. 178). A similar plan is adopted for the *removal of many teeth* or for *removal of jaw or*

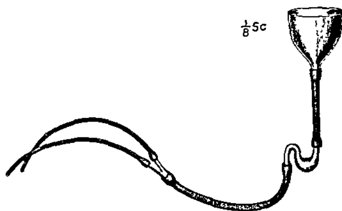


Fig. 179.—Apparatus for administration of ether by the nose.

tongue, except that it is often best to produce the initial anæsthesia with C.E. mixture. When it is not convenient to continue with chloroform through a tube at the side of the mouth, the anæsthetic must be given through a nasal catheter (p. 725). Ether may be used throughout in these cases by means of the apparatus shown in Fig 179. *Tonsils and adenoids* may be removed under "gas" or ethyl-chloride when the surgeon desires a rapid operation. A Doyen's gag (Fig. 180) is to be inserted before applying the face-piece, that time may not be lost in opening the mouth. When a longer operation is required, as for enucleation of tonsils, a deep narcosis, obtained by giving free ether to the point of widely dilating the pupils, may be employed. The position of the patient during the operation must then ensure against the possibility of blood entering the larynx. The head should rest on the occiput, the neck being over-extended on a sand-bag lying behind the nape. When the operator requires the head and shoulders to be raised during operation, it chloroform is, inadvisedly, used the anæsthesia must not be so deep as to abolish the corneal reflex. Moreover, whenever in these operations the head is kept to the middle line, either an active

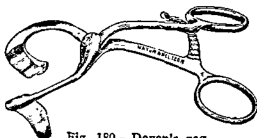


Fig. 180.—Doyen's gag.

coughing reflex is to be retained or else blood must be frequently sponged out from the pharynx. Whenever the surgeon can operate with the patient turned on to one side, then a deep anæsthesia may be safely allowed, as there is no risk of inhalation of blood, which in this position will fall into the lower cheek. At the completion of the operation the patient should be turned completely over, face downwards, with the head hanging over the end of the table, so that blood may easily escape from the mouth and nose. Operations upon the inside of the *nose* are managed in the same way. The mouth should, from the first, always be kept open by a small prop or a Doyen gag.

Operations for *cleft palate* are best managed with chloroform throughout. A deep anæsthesia is necessary, and must be very gradually procured. In these cases, in which the infant is usually feeble, it is apt to be accompanied by pallor and gentle breathing. Care is required to keep the lower jaw from falling, the pulse is to be felt frequently, and extremely small quantities of chloroform are to be given, the Junker pump being employed strictly with inspirations only, and never firmly compressed.

Operations upon the *eye* are best performed under chloroform, as congestion is thus avoided. Enucleation, however, in which congestion is unimportant, should be done under full ether anæsthesia. Operations for *squint* also may well be done under ether, deep anæsthesia being secured before the commencement of the operation, after which no further anæsthetic is needed. Operations *within the skull* are best done under ether by open or intratracheal methods, deep anæsthesia being necessary only while the scalp and the dura mater are being cut.

Long operations upon the *neck* are often attended with interruptions to respiration. For this reason it is advisable to avoid unmixed chloroform and to employ C E. or ether by the open method. The same rule applies to operations upon the *thyroid gland*, in which it is also of great importance to preserve a light anæsthesia as soon as the skin incision is past. Cases of exophthalmic goitre are among the most dangerous for general anæsthesia. Deep chloroform anæsthesia is to be avoided. Rectal ether infusion has often been used with success for these neck operations. A preliminary injection of morphia and atropine or similar drugs is given an hour and a half before operation. Half an hour before, a mixture of ether and olive oil is slowly introduced into the rectum, which has been carefully washed out. The maximum dose is 6 oz. of ether to 2 oz. of olive oil, well shaken together. The dose must be regulated according to the weight of the patient. Ether is soon smelt in the breath, and if narcosis is too light a towel over the mouth and nose will deepen it. The colon should be washed out immediately after the operation. Severe *cellulitis of the neck* supplies another group of dangerous cases in which C.E.

or chloroform is the anæsthetic to choose. Either must be used with very free air dilution, and only a light anæsthesia be obtained. "Gas" and ether, ethyl-chloride, and all closed apparatus are highly dangerous in the subjects of this affection, for œdema of the glottis is often present and will be aggravated by any such limitation of the air supply.

Operations upon the *larynx* or *trachea* are to be performed under chloroform. When the administration has to be continued after performance of tracheotomy, this is conveniently effected by pumping chloroform vapour into the tracheotomy tube, the mouth of a tube attached to a Junker's inhaler being inserted into the upper end of the tracheotomy tube. Breathing is very quiet in these circumstances, and care is required to ensure that the squeezing of the pump be not too forcible and that it coincide with the inspirations. When urgent dyspnœa has been present, as in diphtheria cases, respiration may cease when anæsthesia is established. The surgeon should then open the trachea and insert the tube with all possible speed to permit the anæsthetist, by compressing the chest, to re-establish respiration.

In *breast* cases, long administrations of ether are undesirable for fear of subsequent bronchitis. C.E. or ether should be used for the first twenty minutes, and chloroform afterwards, maintaining a light degree of anæsthesia. Many of these operations can be well managed with continuous "gas oxygen," but the anæsthetic tends to increase the outgoing of blood

Long *abdominal* operations are generally best managed with C.E. mixture, or in feeble subjects with open ether. It is rarely that gas and oxygen alone suffice for these cases, although they may be quite enough for a simple affection—for instance, in a woman or a child.

For *rectal* operations, deep ether anæsthesia is best, unless disease of the lungs is present, as in fistula associated with phthisis.

The operation of *circumcision in infants* is best performed under an anæsthesia induced by C.E. or chloroform, and maintained with pure ether on an open mask. A light anæsthesia is all that is required after the removal of the prepuce. Perfect stillness of the lower limbs is only obtained by a very deep anæsthesia in these cases. It is far better to rely on a light anæsthesia and have the thighs controlled by an assistant at the moment of the cut through the prepuce. It is a mistake to think that chloroform is essential for infants; many fatalities have resulted through performing this operation during a deep chloroform anæsthesia.

ETHER

Ether is a transparent, colourless, volatile liquid with pungent odour and burning taste. Its vapour is highly inflammable and, when mixed with air, explodes violently if near a flame. Ether bottles,

therefore, must never be placed near a fire or a gas-jet; the liquid must never be poured out in any such neighbourhood; and ether must not be employed near the actual cautery or diathermy apparatus. Two kinds of ether are available for anæsthetic purposes: (1) ether purificatus (off.), sp. gr. not above 0·722 or below 0·720, obtained from pure rectified spirit; and (2) rectified ether, sp. gr. 0·720, obtained from methylated spirit. Either kind should be neutral to test-paper. The latter is considerably the less expensive. The results obtainable from the two kinds in practice are almost identical. Ethanesal may be regarded as ether for practical purposes.

Ether may be given in two totally different ways, according as *closed* apparatus is used or the *open* method employed. Each method has its advantages and its disadvantages. In the case of the closed method, by initiating the ether administration with nitrous-oxide or ethyl-chloride, patients can be anæsthetized without tasting the ether at all during the period of induction—in some cases a great advantage. Unconsciousness is quickly attained in this way, without the escape of any great amount of ether vapour into the air of the room. Moreover, the most difficult subjects can be anæsthetized. On the other hand, there is in many cases a certain amount of cyanosis, of spasm, and of mucous secretion, all of which are less when the open method is used. The latter method also is very much simpler, as well as safer. It is to be preferred, therefore, by those who use ether as a routine anæsthetic in all cases, although it is not efficient in the case of very alcoholic, robust subjects without the expenditure of much time and the prolongation of the excitement stage.

Administration by the **open method** is thus conducted: A mask, similar to that used for C.E. (p. 704), though sometimes of a larger size, is covered with ten layers of fine gauze or two layers of the flannel used in the case of C.E. A face-pad of gauze, made by tying together the two ends of a roll about an inch thick and one and a half feet long, is laid upon the patient's face so that the whole of the mouth and nose are within the circle of gauze. The mask is then placed lightly on the face, resting on the gauze pad, and the patient is told to breathe gently in and out of the mouth. After a few breaths ether is added drop by drop from a drop-bottle of the same kind as that used for C.E. At first only the lower part of the mask is moistened, but after three minutes, as the patient becomes accustomed to the vapour, and if his breathing is uninterrupted by coughing or holding of the breath, the ether is added freely until the whole surface of the mask is kept saturated. *Excitement is not* a marked feature of the induction, and objection to the vapour is less than might be expected, provided that the ether is dropped on in sufficiently small quantities during the first minutes. When anæsthesia

is established it is not necessary, except in the case of difficult subjects, to add ether freely, perfect immobility being usually maintained if the drug is steadily added by drops. A considerable amount of ether vapour escapes into the surrou[illegible] to those engaged upon the case. [illegible] another is the large amount [illegible] must be plentifully supplied with the drug if a long case is anticipated; 10 oz. is frequently required in such circumstances.

This method of giving ether can be adopted for use in long operations about the mouth or nose, as, for instance, removal of the tongue, for which the closed method is unavailable. To use ether in these cases it is necessary to be supplied with the apparatus shown in Fig. 179. When anæsthesia has been established by the open method, the pharynx and pharyngeal aspect of the epiglottis and larynx are brushed with a 2 per-cent. solution of cocaine. The rubber tubes are passed into the nares till the lower ends are opposite the epiglottis. The pharynx is now packed with a roll [illegible] is held forward. Anæsthesia is [illegible] the flannel closing in the glass [illegible] for long operations within [illegible] the mouth and the oral [illegible] difficult subjects the use [illegible] by a hypodermic inj[illegible] half an hour before [illegible]

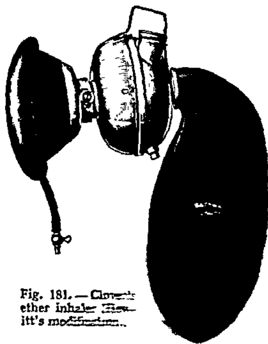


Fig. 181.—Clover's ether inhaler, Hewitt's modification.

For using eth[illegible] been devised, all [illegible] —viz. restricti[illegible] vapour. We [illegible] (Fig. 181)—[illegible]

consists of three main parts: a face-piece that is screwed on to the ether reservoir, on to the top of which fits a bag. There is an opening, through which ether is poured to charge the inhaler; this is closed by a glass stopper. By movement of the regulator, inspirations at the face-piece are allowed to traverse the ether in increasing degrees, so that, when an inspiration is drawn through the apparatus with the indicator at "½," one-half of the inspired air passes over the ether, but if the indicator is at F the whole must pass in this way. Before use the inhaler should be warmed. An ounce and a half of ether is then inserted with the indicator at ½, the stopper replaced, the indicator moved to 0, and a long breath blown through the inhaler from the face-piece to clear out any ether vapour that may have escaped into the central shaft. The face-piece must be screwed on to the reservoir in such a position that when the inhaler is in use the opening for pouring in ether looks upwards. The narrow end of the face-piece corresponds with the bridge of the patient's nose.

Being now charged with ether, but freed from any smell of it, the inhaler is applied to the face in such a way that, though there is no leakage of air around the edge of the face-piece, yet this does not press heavily upon the patient. The face-piece is grasped firmly by the anæsthetist's left hand, the little finger of which rests behind the angle of the patient's lower jaw on the left side, his head being turned to the right. The anæsthetist's right hand serves to regulate the degree of pressure which the inhaler bears upon the patient's face, and also to move the indicator for admission of ether vapour. The patient is asked to breathe in and out of the mouth, and during the first two breaths the face-piece is just raised during inspiration and closely applied during expiration. Thus the bag is distended. Then the face-piece is allowed to rest on the face continuously, and the indicator is slowly moved from 0 towards F. At first this is done so slowly that at least a minute is spent before ¼ is reached. Any coughing or holding of the breath at this time shows that the indicator is being moved too fast, and it is put back. At the end of about three minutes, the indicator being at ½, consciousness will be abolished and the indicator may be pushed on more rapidly. For an adult man it is pushed on to F and kept there until the skin incision has been made, when it is brought back to ½. In the course of long operations it is often brought back to ¼, or half-way between that and 0. When stertor is first heard, the face-piece is raised during one inspiration and reapplied. There must be no hurry to admit air before this point is reached, even if a little duskiness of the face is incurred, as prolonged excitement in the induction stage is apt to follow. When anæsthesia has been reached, the face-piece is raised sufficiently often, generally

about once in every five breaths, to keep the colour free from cyanosis by admission of breaths of air. In "easy" subjects the bag may be left off entirely, air being thus freely admitted throughout.

By **preceding ether with nitrous-oxide**, anæsthesia can be induced without the unpleasantness of ether vapour becoming apparent to the patient. The procedure is best executed by the apparatus and the manœuvres just described, with slight modification. Thus the small bag is not used at first, but is replaced by that figured in Fig. 182, which is connected with a cylinder of nitrous-oxide. No ether is poured into the reservoir until the patient has inhaled six breaths of nitrous-oxide. During this time the expirations are allowed to escape by the expiratory valve shown in Fig. 182. This is then closed, and without moving the face-piece the stopper of the ether reservoir is removed, 1½ oz. of ether is inserted, and the stopper replaced. The indicator is then moved as in the administration of ether alone, so that the patient will be breathing to-and-fro an atmosphere of nitrous-oxide with constantly increasing additions of ether vapour. When the point ½ is reached, the gas bag is replaced by the small bag and anæsthesia maintained as with ether alone.

When it is desired to **precede ether with ethyl-chloride** a small bag must be used, fitted with a tap (Fig. 185). This bag is fitted on to the top of the ether reservoir, and the administration is begun exactly as described on p 720. After the fourth breath the necessary ether is inserted and the indicator rapidly pushed along, so that an ether anæsthesia supervenes upon that of ethyl-chloride without any interval of consciousness. As soon as stertor arises the small bag should be lifted off during three breaths, and squeezed free of any ethyl-chloride vapour within it. It is then placed on again during the expiration, and the administration goes on as in the case of ether only.

Ether is sometimes administered by what is known as the **semi-closed** method. For this purpose an inhaler such as that of Allis or of Rendle is employed, whereby air supply is to some extent restricted, the strength of the vapour supplied being graduated only by the varying proximity of the inhaler to the face. In our opinion this method never has any advantage over one or other of those just described

Rectal administration of ether is described on p. 711.

NITROUS-OXIDE

At ordinary pressure and temperature nitrous-oxide is a colourless gas with sweetish odour and taste. It is supplied in the liquid form within strong cylinders under a pressure of 50 atmospheres. Fifteen ounces of the liquid furnish 50 gallons of the gas, and if the cylinders are securely jointed the liquid will keep for an indefinite period. Intense

cold accompanies the conversion of the liquid into gas, therefore care must be taken not to liberate it too fast from the cylinders lest freezing occur about the joint. After a cylinder has been used, the liberating screw must be turned off again very thoroughly to prevent loss of the gas by leakage. When given pure, nitrous-oxide affords an anæsthesia of about half a minute. Its full anæsthetic effect is accompanied by spasmodic obstruction in the upper air-passages, cyanosis, clonic and sometimes tonic muscular contractions. By the use with nitrous-oxide of air, or of oxygen, these phenomena, which necessitate the removal of the anæsthetic, may be postponed or greatly diminished, and hence a longer inhalation of nitrous-oxide is rendered possible. A proportionately longer anæsthesia is thus obtained. The combination of oxygen with nitrous-oxide requires special apparatus and considerable practice to ensure good results. Its advantage over that of air and nitrous-oxide skilfully employed is not sufficient to recommend it, except to the expert who has much practice and to whom the additional apparatus is not a formidable obstacle.

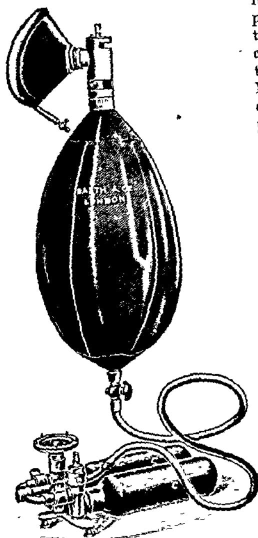


Fig. 182.—Apparatus for administration of nitrous-oxide gas.

The apparatus (Fig. 182) for giving nitrous-oxide, pure or with air, consists of two side-valve cylinders, c, c, each yielding 25 gallons, with stand, double union, and foot-key. For hospital work cylinders of 50 or 100 gallons are generally used. These are joined by an india-rubber tube to an india-rubber bag capable of holding 2 to 3 gallons of the gas. This bag connects with the face-piece by Hewitt's valved stopcock. The cylinders are not to be used alternately, but the

foot-key is kept on one, and this is used till it is exhausted. The other is then brought into use, and the empty cylinder replaced by a full one. The full cylinder should be tested by weight before being used, to see that the weight stated on the label is correct. The sound which a full cylinder gives when struck with a metal instrument is different from that given by an empty cylinder treated in the same way.

Before use the apparatus is to be tested by turning the foot-key, letting a little gas into the bag with the stopcock closed, and pressing it out of the open expiratory valve. The foot-key is turned by pressing firmly on it with the left foot and rotating the knee outward. Before starting to administer, put the cylinders into such a position that the foot-key is easily reached and worked when the face-piece is being held to the patient's face. Then, with the stopcock "off," fill the bag about two-thirds full. The patient having been examined in the ordinary way (p. 701), a small prop (Fig. 172)—or, if necessary in a dental case, a larger one—is placed between the teeth; the head is allowed to rest in a suitable position, neither flexed nor extended, but in its natural relation to the chest; and the face-piece is gently applied, so that it fits the face accurately, the apex resting on the bridge of the nose and the broad end on the chin. The sound made by the valve working as the patient breathes in and out will show that the face-piece is properly applied. If there is a moustache or beard, the hair should be moistened with water where it comes into contact with the face-piece. This is held by the anæsthetist's left hand, with the little finger pressing up below the patient's chin. Two fingers of the right hand are employed to keep the rim of the face-piece closely pressed against the bridge of the nose, where air leakage is most likely. The patient is asked to breathe freely in and out of the mouth. The stopcock is then turned on with the right hand, and nitrous-oxide is thus admitted from the bag to the patient's mouth. At the same time the foot-key is worked so that gas gently streams into the bag. The gas is now being inhaled from the bag and expired into the air. After about half a minute consciousness goes, the breathing is deeper and quicker than natural, the face becomes dusky, and the pupils dilate. After some twenty to thirty breaths, jerky, guttural, stertorous respiratory noises demonstrate the presence of anæsthesia, and, in the case of a very short operation, afford an indication to remove the face-piece. If a slightly longer anæsthesia is desired, the expiratory valve should be closed and re-breathing for a few breaths be allowed.

An administration such as this suffices for such procedures as extraction of two or three teeth, or the opening of an abscess.

The conjunctival reflex is abolished, but not the corneal. Muscular twitching or jactitation or opisthotonos, or pallor (a rare

occurrence), if they arise, must be regarded as signals to stop the administration.

If the operation is not one within the mouth, the occurrence of any of these phenomena, stertor, twitchings, etc., is the signal to allow the operation to begin. Air is then admitted, by turning off the stopcock, until the stertor has subsided. Usually two or three breaths suffice. Gas is readmitted now by again closing the stopcock; and in this way, by giving regular breaths of air alternating with every four of nitrous-oxide, anæsthesia may be kept up as long as desired. The longer the administration lasts the shorter must the intervals be between the admissions of air. The anæsthetist must be guided, however, by the patient's colour and his manner of respiration. Different types of individual require different proportions of nitrous-oxide and of air. Thus, whereas muscular, high-coloured, and alcoholic individuals must be scantily treated as regards air-admission, this must be freely practised, and begun before stertor arises, in the case of children and of the anæmic and the feeble. Intervals of apnœa not uncommonly arise in the course of long nitrous-oxide inhalations. A stoppage of respiration in such circumstances must not alarm the anæsthetist. He must remove the face-piece, tilt up the chin, and, if respiration is not resumed, press on the chest. Breathing will begin again without any deleterious effects being produced. The condition is different from, and without the dangers of, that seen when respiration ceases during the inhalation of chloroform and other anæsthetics.

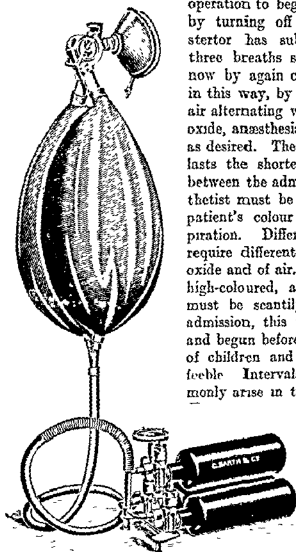


Fig. 183.—Hewitt's apparatus for "gas and oxygen."

For giving nitrous-oxide with definite percentages of oxygen the procedure is similar to that described, but special apparatus (Fig.

183) is necessary. When the face-piece is applied and the patient is breathing *satisfactorily through the mouth*, the indicator is at once put to 2. The figures marked upon the metal mixing-chamber indicate roughly the percentages of oxygen admitted by moving the indicator; thus a mixture of 98 per cent. nitrous-oxide and 2½ per cent. oxygen will now be inhaled. After four breaths the indicator should be advanced to 3, and by the end of a minute it should be at 6. Anæsthesia is not marked by any violent stertor, such as is heard with nitrous-oxide alone. *A gentle snore, accompanied by* absence of conjunctival reflex, flaccidity of muscles, and a fixed or slowly oscillating condition of the eyes, is the usual sign of anæsthesia. The pupils are generally of moderate size. Excitement, if present, indicates that oxygen is being too freely used, and the indicator will then be pushed back towards the N_2O mark. On the other hand, blueness or jactitation calls for more oxygen, and in *the course of prolonged operations as much* as 20 per cent may be needed, 10 per cent. being an amount commonly required.

In order to permit the performance of a moderately long operation within the mouth, such as extraction of many teeth, under nitrous-oxide anæsthesia, apparatus has been devised for the administration of "gas," and also of "gas" and oxygen, through the nose. The use of this, however, is only occasionally desirable, requires special practice, and can always be well replaced by ether anæsthesia. Space, therefore, will not be given here to a description of the nasal administration of nitrous-oxide.

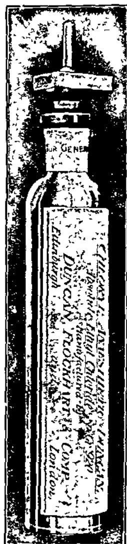


Fig. 184.—Ethyl-chloride tube.

ETHYL-CHLORIDE

Ethyl-chloride (C_2H_5Cl) is supplied in hermetically sealed glass tubes, from which it is liberated in the form of a spray by means of spring taps of various kinds (Fig. 184). It is inflammable and not to be used near a naked flame; it must be pure, and consequently that sold for local anæsthetic purposes is not usually fitted for producing general anæsthesia;

and it should be used only as a preliminary to other anæsthetics (*see* pp. 715 and 721), or else for such operations as can be done in a few minutes after the inhalation of a dose sufficient to produce anæsthesia.

The administration is thus conducted: A small prop is placed between the patient's teeth, because of the frequency with which severe jaw-spasm arises. A dose of ethyl-chloride (2 c.c. for children up to four years of age, 3 c c. up to ten, 4 c.c. for older children and

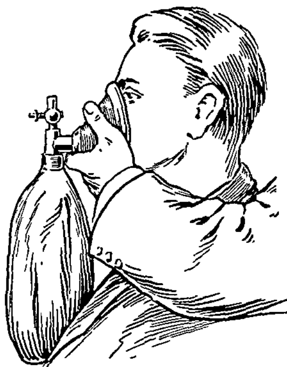


Fig. 185.—Administration of ethyl-chloride from small bag of Clover's inhaler.
(*Blomfield's "Anæsthetics"*)

women, and 5 c.c. for men) is sprayed into the bag through *its top.* The face-piece is gently adapted to the face so as to catch an expiration *and then remain in close contact. The patient is asked* to breathe quietly only, and the bag, which was at first allowed to *hang at right angles to the opening of the face-piece,* is during three breaths raised till it is at right angles to the face (Figs. 185 and 186). After the third breath the face-piece is lifted off the face during one inspiration and closely reapplied to catch the expiration. Unconsciousness supervenes with remarkable rapidity and quietness. Children are often unconscious after the second breath from the bag, and adults after four or five breaths. The face is flushed, with-

out any blueness. There may be no stertor, and the fixed position of the globes, with a dilated pupil and absence of conjunctival reflex, is the best indication of anæsthesia. The corneal reflex should not be abolished. When anæsthesia is reached the apparatus is removed.

Ethyl-chloride is not well adapted for the maintenance of a prolonged anæsthesia. An anæsthesia lasting between one and two minutes is generally obtainable from a single dose. Recovery of con-

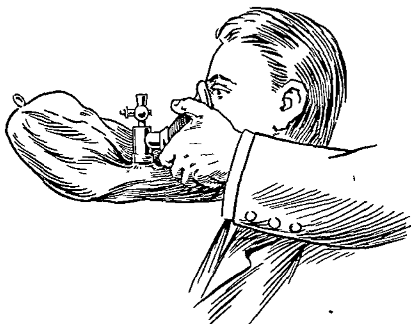


Fig. 186 —Administration of ethyl-chloride from small bag of Clover's inhaler.
(Blomfield's "Anæsthetics")

sciousness is rapid, but is more often accompanied by sickness or by headache than is the case with nitrous-oxide. Moreover, faintness is sometimes a sequel, and fatal collapse has occurred in several recorded instances. Ethyl-chloride is therefore not to be regarded as on the same footing of safety as "gas," and, in spite of its great convenience and extreme rapidity of action, should never replace nitrous-oxide when this is available and suitable. Careful limitation of doses employed, early admission of a breath of air, and the lying-down position of the patient, are probably the most important points to be observed for securing safety with ethyl-chloride.

In addition to its employment in the manner described, ethyl-chloride is sometimes used upon an open mask as a preliminary to

C.E. or to chloroform. The object, then, is not to produce absolute anæsthesia with ethyl-chloride, but to induce rapidly an unconscious or semi-conscious condition during which the more formidable drug may be inhaled without inconvenience. The ethyl-chloride in such cases is sprayed straight on to the open mask or on to the sponge of the semi-open inhaler in use. Owing to its free dilution with air the dose of ethyl-chloride need not be so strictly limited as when closed methods are employed. This preliminary use of ethyl-chloride on an open mask is very convenient for safely and quickly quelling the cries of a frightened infant when desired.

CHLOROFORM

Chloroform ($CHCl_3$) is a colourless liquid, less volatile than ether, with a sweetish, fiery odour and taste. It is not inflammable, but in the presence of naked flame its vapour decomposes, forming poisonous compounds (carbonyl-chloride). For this reason there should be free ventilation whenever chloroform is used in a small room containing a fire or a bare lamp-flame or gas-jets. It should be stored in a cool, dark place, and its purity should be evidenced by neutral reaction to test-paper, non-irritating smell, and absence of residue on spontaneous evaporation from a watch-glass. Upon nerve tissue chloroform has a deadening action about seven times as powerful as that of ether. It produces, when in the circulation, lowering of blood-dressure and weakened heart-action and gradual failure of the vital centres. The stronger the vapour of chloroform inhaled, the more certain and rapid is the production of these effects. The cardinal principle, therefore, in the administration of chloroform is to supply a vapour freely diluted with air; and from experiments, both clinical and physiological, it is concluded that about 2 per cent. of chloroform to 98 per cent. of air is the safe strength. For induction of anæsthesia it may be, and often is, necessary to exceed this strength. For the maintenance of anæsthesia when once induced that is rarely the case

The importance of regulating the strength of vapour of a drug so potent as chloroform has led to the invention of many instruments designed to achieve this aim. It is certain, however, that even with such instruments constant care and watchfulness on the anæsthetist's part are necessary for safety when chloroform is used. Consequently, many anæsthetists still prefer simple means of administration, relying for the avoidance of accident upon close observation of the symptoms evoked, and their knowledge of the danger of strong vapours. Moreover, the simple methods are more widely applicable and infinitely more convenient. We shall therefore describe such a system of administration first, as being one on the whole most suited to a competent

anæsthetist. The inexperienced, however, will undoubtedly run less risk of accident if he employ a regulating inhaler.

The **most simple and most efficient method of giving chloroform** is by means of a drop-bottle and open mask. Those used in the case of C.E. (p. 704) are perfectly applicable here. The principle of gradual administration is to be strictly adhered to, and the amount of liquid allowed to fall upon the mask is to be very much less than in the case of C E. Moreover, only one layer of thin flannel is to be used on the mask, and the mask should *never rest upon the face.* Only by observing this rule can the certainty of not supplying an overdose be secured. Should the mask rest upon the face, then by comparatively complete exclusion of air even small quantities of chloroform dropped upon the mask will soon raise the strength of the vapour inhaled to a dangerously high percentage. On the other hand, if the mask does not touch the face, even if its covering is wet throughout with chloroform, there will be such dilution provided by the air between the mask and the face that danger of overdose is not likely

In employing this method of administration, then, begin with the mask held a couple of inches off the patient's face, which is turned on one side. Breathing being smoothly and regularly in progress, allow ten drops to fall upon the centre of the mask. Let this gradually approach the face till at the end of a minute it is at a distance of half an inch. During the second minute allow twenty drops to fall on the mask, still keeping this just off the face. From the end of the second minute add the chloroform more freely, till at the end of the fourth minute the lower half of the mask is kept moist. By this time the patient, who may have been talking incoherently, will probably be quite unconscious, although all the reflexes will remain active. There may be also some sitting-up movements and some rigid extension of arms and legs. Keep the lower half of the mask, which still does not touch the face, uniformly moist, rub the lips if there be holding of the breath, and by the end of the sixth to eighth minute snoring breathing will denote the advent of anæsthesia. It is important that the administration should be continuous, not intermittent. The muscles of the limbs will now be relaxed; the pupil will be of small medium size, reacting to light; the conjunctiva insensitive; and the corneal reflex present, but less brisk than in the conscious subject. Anæsthesia is now deep enough for the majority of operations. For abdominal cases, however, or for those on especially sensitive parts, such as the ends of the fingers and toes, urethra, etc., it should be carried still farther before the initial incision is allowed. In these cases the corneal reflex should be abolished, the pupil being kept small

In giving chloroform by this method, it is most important to bear in mind—

1. That chloroform is most rapidly absorbed during the first two minutes of inhalation; therefore the quantity offered for inhalation during this period must be most carefully restricted.

2. That during the period of spasm, with holding of the breath, which not uncommonly arises in the early minutes, no attempt must be made *to press the chloroform. If this period is prolonged, use* ether until it has passed, as in the administration of C.E. (p. 705). *This is especially to be recommended in the case of robust or alcoholic* subjects.

3. *That the mask should not be permitted to touch the face,* and that in the course of a long operation the amount of chloroform used should be reduced till *only a very small portion of the mask* is kept moist.

The anæsthetist must *aim at offering a uniformly weak vapour*, not at giving now a considerable amount of chloroform and *now none* at all. Consequently he should be careful repeatedly to add very small amounts, not to pour on a drachm or two and then wait some minutes before re-moistening the mask.

The use of some of the **regulating inhalers** which have been invented in order to overcome the difficulty of ensuring by the above simple method a constant and highly diluted vapour must now be briefly described. These inhalers are for the most part made upon one of two different principles, which are known as the *plenum* and the *draw-over* or *vacuum*. In the plenum class of inhaler a mixture of chloroform vapour and air of definite proportions is pumped on to a face-piece for inhalation by the patient (Waller, Alcock, Roth-Drager, Dubois, etc.); whilst in the vacuum type the patient's respirations draw air over or through chloroform (Vernon-Harcourt, Levy, etc.). Thus, in the former class the manner in which respiration is conducted is entirely independent of and makes no difference to the vapour supplied, this depending simply on the mechanical means. In the latter class, however, this is not the case, the patient drawing air through the apparatus—that is, over the chloroform—by means of the respiratory muscles. This process lends itself to the construction of a small and compact instrument. It has, however, the disadvantage that it places ome obstruction in the way of free respiration, and that the percentage of chloroform is affected by the vigour or feebleness of the respiration.

Junker's inhaler (Fig. 187) differs from other plenum apparatus in that there is no record on the instrument of the chloroform percentage offered for inhalation. This applies also to Shipway's warm-vapour apparatus. It is not possible to know with this instrument the exact

strength of the vapour that is being delivered; and if the compressions of the ball-pump do not exactly coincide with inspiration, or if they are not kept at moderate strength, it is possible to deliver a vapour of undesirably high percentage. Nevertheless, its use in unskilled hands is probably less dangerous than that of the drop-bottle. For cases in which chloroform has to be delivered through a tube in the mouth or a catheter in the nose, as in long *tongue and laryngeal cases*, this instrument or that of Shipway is invaluable. In such cases anæsthesia is first induced in the ordinary way—by "gas" and ether, or C.E., or whatever drug the anæsthetist has decided upon as best in the particular case. A full degree of anæsthesia having been reached before the operation is begun, the Junker should then be brought into use. If, for instance, the tongue is to be removed, a nasal catheter will be fitted

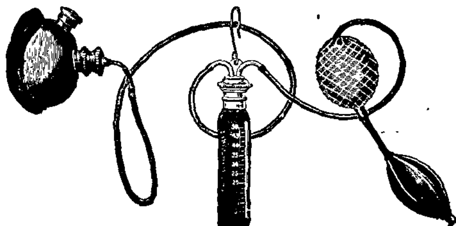


Fig. 187.—Junker's chloroform inhaler.

on to the exit tube and passed along one nostril till the end of the catheter overhangs the glottis, as ascertained by a finger passed to the back of the mouth. The other nostril should then be plugged with a strip of gauze. With each inspiration a gentle compression of the india-rubber ball is made. In this way a constant chloroform anæsthesia will easily be maintained, and the anæsthetist will be able to keep entirely out of the surgeon's way. If by reason of nasal deficiency a catheter cannot be conveniently used, the metal tube is to be placed inside the mouth, well back on the side opposite to that of the tongue lesion. Both nostrils should be plugged with gauze. Neglect of this plugging-up of respiratory orifices, other than that into which the chloroform is being pumped, often renders it difficult to maintain quiet anæsthesia in the case of bad subjects.

When used for *ordinary cases*, as opposed to those concerning

mouth, nose, and throat, the exit tube of the Junker inhaler is fastened to a metal frame over which stretches a single layer of flannel. This mask is closely applied to the face, and after a few breaths have been drawn, to accustom the patient to the mask, a very gentle compression of the india-rubber ball is effected coincidently with each inspiration. The strength of the compressions should gradually be increased, as much time (six to eight minutes) being occupied in inducing full anæsthesia as when the drop method is employed.

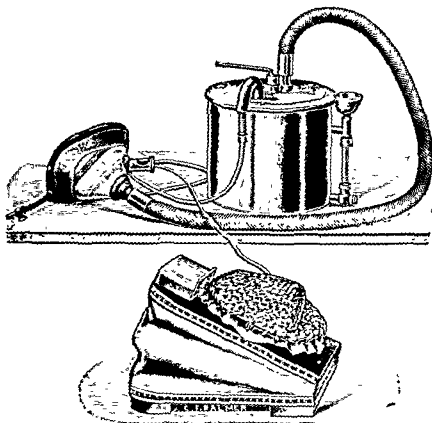


Fig. 188.—*Alcock's regulating chloroform inhaler.*

The other inhalers of the plenum type, with the exception of Shipway's, though more accurate instruments than the Junker, suffer from complexity and lack of portability. They are excellent for use in institutions where portability is not required, and one or another should be available wherever students are taught the use of chloroform. Alcock's apparatus, as being the most convenient, may be briefly described. It consists (Fig. 188) of a circular copper vessel, 5 in. in diameter and $4\frac{1}{2}$ in. deep, which contains 150 c.c. of chloroform. A shelf, closed except for two oblong holes, is fixed $1\frac{1}{4}$ in. from the bottom of this chamber. Directly above and touch-

ing this shelf is a circular plate, movable by means of a hollow rod in the centre, and pierced by two triangular apertures. These can be adjusted by the central rod to expose more or less of the oblong holes in the shelf, and so produce larger or smaller openings intc the space below. Air (supplied from a small foot-bellows or from an electric fan) enters the chamber by a tube opposite one aperture and leaves by another tube opposite the other, taking up more or less chloroform vapour according to the size of the apertures. *A thermometer in the hollow rod* indicates the temperature of the chloroform below, and a water-jacket surrounding the chamber keeps the temperature between certain limits.

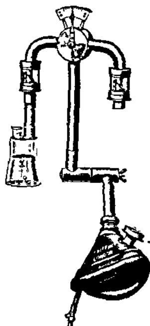


Fig. 189.—*Vernon-Harcourt's chloroform inhaler.*

The best-known inhaler made on the vacuum principle is that of Vernon-Harcourt (Fig. 189), the features of which may be understood from the figure. In using this instrument, important points to observe, in order that the vapour inhaled may correspond with the strength registered on the dial, are (1) to hold the face-piece in perfect adaptation to the face, allowing no air-entry around one edge, and (2) not to shake the instrument to any considerable extent. The inhaler admits of a maximum percentage of 2, but this can be increased to 2·5 or 3 by means of a small tube which is provided to fit on to the open neck of the bottle. Even so, however, there are instances, in the case of difficult subjects, when with this apparatus induction is unpleasantly tedious.

POSITION OF PATIENT

The routine position for the patient during anæsthesia has been mentioned, but there are *certain cases in which it cannot* be adopted and in which the position given to the patient's head or trunk is a matter of prime importance, both as regards safety and the surgeon's convenience. These must be briefly dealt with.

First come all those cases in which in the course of operations blood enters the mouth, pharynx, or posterior nares, and may be inhaled. In all such cases, of which tonsil and adenoid operations provide the most familiar examples, the patient should be placed completely on his right side, if the surgeon can operate in that position. If he

finds it necessary to have the head in the middle line, then only a light anæsthesia, which allows of coughing, or else repeated sponging away of blood, is to be resorted to; or the procedure indicated on p. 709 may be adopted. In long operations upon the tongue or upon the inside of the nose the same rule applies, but here it is often possible, by means of a sponge inserted at the back of the mouth, to exclude blood from the glottis and to permit of deep anæsthesia, even with a patient on his back and his head straight, or in a semi-recumbent position, as the surgeon chooses. In cases of empyema, where there is only one freely acting lung, it is essential that this should not be embarrassed. Usually, therefore, the patient must be placed, so far as the operation permits, upon the affected side. By drawing him well to the edge of the table, so that his ribs almost over-hang it, the surgeon can generally get at the required spot. In operations for intestinal obstruction one shoulder should be raised upon a sand-bag and the head turned to the opposite side with the mouth slightly opened. If any quiet regurgitation of the fluid takes place, as is not uncommon in these cases, it will then escape; in the dorsal position there is great danger of inhalation when such fluid suddenly floods the mouth and nose. The *Trendelenburg position*, with pelvis raised and head and shoulders low, is often adopted for pelvic operations, and by some for tongue cases. It is a very safe position from the anæsthetist's point of view, and one in which chloroform is generally much to be preferred to ether.

In all positions the anæsthetist should see that there is no risk of paralysis of any muscle or limb from undue pressure against the hard edge of the table or from the over-stretching of nerve trunks.

PREPARATION OF PATIENT FOR, AND TREATMENT OF, AFTER, ANÆSTHESIA

In the case of nitrous-oxide no preparation is necessary, but the last meal should have been taken at least two hours before the inhalation, and the bladder should be emptied. In the case of all other anæsthetics it is advisable that the administration take place at least four hours after the last taking of food. A purge thirty-six hours and an enema two or three hours before administration is the usual practice. Some persons, however, are much upset, even to fainting, by enemata, which therefore should be omitted in such cases. In the case of infants, an operation should be performed at an hour that normally would be feeding-time; at the next feeding-time half the ordinary food is allowed. In an operation involving a considerable period in bed afterwards, it is well that two or three days be spent in bed beforehand; the patient gets accustomed to nursing routine,

and also to lying quietly. Before many abdominal operations careful choice and restriction of diet are of advantage, as well as systematic cleansing of the mouth and pharynx with mild antiseptics. After these operations, as a rule, the minimum amount of food should be taken by the mouth during the first twenty-four hours. Small quantities of tepid water are allowed after four hours, and a cup of weak tea after eight hours. Enemata of one pint of normal saline solution are given slowly every six hours.

After-sickness may sometimes be obviated by the addition of 10 grains of aspirin to the first saline enema, aided by the adoption of the sitting position, if permissible. The suspicion of "delayed chloroform poisoning," as suggested by repeated sickness in a child, should be treated by washing out the stomach and leaving in it 2–4 ounces of a solution of sodium bicarbonate (10 gr. to the ounce) in 80-per-cent. glucose.

The unpleasant taste of ether, if it clings about the mouth, will often be neutralized by permitting the patient to suck lemon-peel.

Careless moving of the patient back to bed after operation is often responsible for the initiation of vomiting. It should be done with as little jolting or rolling of the patient as possible, and with careful support of the head. The best routine position in which to lay the patient during the period of "coming round" is on the right side, with the head and shoulders raised on one pillow.

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LOCAL ANÆSTHESIA

By GWYNNE WILLIAMS, M.D., M.S., F.R.C.S.

AND

F. S. ROOD, M.B., B.S.

Historical ... tical begin- ... is drug was ... he domains of rhinology and laryngology. In all these it is still predominant as compared with other departments of surgery. In the regions of the eye, nose, and larynx, anæsthesia was induced by the local application of the drug to the surface. The next step was the injection into the tissues of solutions in strengths varying from 2 to 20 per cent.; but as this method, although successful in producing anæsthesia, led to pronounced and sometimes fatal toxic effects, attempts were made in various directions to obviate this drawback.

First, Schleich used a solution so dilute as 0·2-per-cent. cocaine in a hypotonic salt solution, believing that the hypotonicity aided the anæsthesia; but H. Braun has shown that the required effect can be produced just as easily with 0·2-per-cent *cocaine in an isotonic salt solution*, which, of course, has the advantage that it does not damage the tissues. Secondly, Corning ... anæsthesia in ...

... practicable in the limbs, and it was not until the discovery of the ... constrictor effect of extract of the suprarenal gland that local analgesia could be used satisfactorily for major operations requiring protracted anæsthesia. This drug, by producing an anæmia of the part, slows the absorption of the anæsthetic into the general circulation, and by keeping it at the site of injection prolongs the duration of the anæsthesia. Lastly, various derivatives *of cocaine and other drugs have been prepared*, of which the best-known are tropacocaine, β-eucaine, and novocain; they are undoubtedly less toxic than cocaine, but are not equal to it in their local anæsthetic properties. For purposes of injection they have practically displaced cocaine.

Local anæsthesia can be produced in the following ways:—

1. *By application of the drug to the surface* to be anæsthetized, e.g. the nasal mucous membrane.

2. By infiltration of the area of operation.
3. By injection into or around the nerves going to the part to be operated upon (endoneural or perineural method, sometimes called regional).
4. Injection into the vessels of the part, more especially into the veins (Bier).

1. Superficial application.—For the production of anæsthesia of the mucous membranes by the simple local application of the drug, cocaine has remained by far the most efficient agent, none of the other preparations having the same effect. For the nose and the air-passages a solution of from 5 to 20 per cent. is used, applied by means of a spray, or by swabs of cotton-wool. It is important in this case not to anæsthetize too large an area at one time, lest an idiosyncrasy exist on the part of the patient towards the drug. The urethra and bladder can also be anæsthetized by the introduction of the solution, but here the danger of cocaine-poisoning seems to be greater, so that only very dilute solutions, e g. 1 to 2 per cent., should be used, or novocain substituted. In the anæsthetization of mucous membranes for operative procedures, apart from mere examination, it is well to add adrenalin solution for the double purpose of prolongation of the cocaine action and of lessening the risk of toxic effect, while in addition its hæmostatic effect is of great value.

The surfaces of granulating wounds can also be rendered insensitive by the application of 5- to 10-per-cent. cocaine, or 5-per-cent. carbolic acid; while for non-operative purposes the dusting of the wound with orthoform is very satisfactory.

2. Infiltration method.—This consists essentially in soaking the area to be operated upon with anæsthetizing solution. For small areas it is usually very satisfactory, but in larger areas an attempt is made to combine it with regional anæsthesia by directing an injection into the proximity of the nerves going to the part.

With regard to the solution to be used, Braun recommends a series containing varying strengths of novocain and adrenalin—novocain 0·25–2-per-cent., adrenalin (1 . 1,000) 5–20 drops in 100 c.c. of water. He uses the stronger solution when he wishes to infiltrate around the larger nerve-trunks, the weaker when large areas have to be injected with the solution. For local infiltration and regional anæsthesia, novocain has displaced all other drugs. It is practically non-toxic. It is usual to use stronger solutions than formerly, 2-per-cent. being commonly employed for both regional and infiltration anæsthesia, and 10 drops of a 1 : 1,000 adrenalin solution are added to each 100 c.c. of novocain. A 2-per-cent. novocain solution produces a very profound anæsthesia in the area infiltrated. It also cuts off the conduction in the nerve-trunks passing through this area, so that a

secondary area of regional anæsthesia rapidly develops by the side of the infiltrated patch distal from the central nervous system. This is a great advantage in some situations, such as the back, thigh, and buttock, where the anatomical distribution of the nerves is such that it is not easy to localize them accurately; so that instead of having to infiltrate the whole area of operation, a broad linear injection or a ring round the required area is generally sufficient. As much as 250–300 c.c. of 2-per-cent. novocain may be injected into an adult without danger, and in operations such as the radical cure of large umbilical hernias, for which this form of anæsthesia is especially suitable, this amount will probably be required.

Preparation of the patient.—As a rule, the patient need not be starved; but if there is any reason to suppose that the local anæsthesia will be insufficient and a general anæsthetic required, preparation for the latter should be made. In nervous patients it is advisable to give an injection of morphia and scopolamine forty-five minutes before the operation

The patient should always be in the recumbent position, since the psychical effect of the operation occasionally brings about a fainting attack, which at the same time alarms the patient and interferes with the operative procedure.

Technique of the injection.—By far the best syringes for this purpose are the ordinary glass Record syringes with metal pistons. Detachable needles of all sizes are made to fit them. The whole of the infiltration is done with a sharp needle. Even if a vessel is punctured with a fine needle no harm will result. A few insensitive spots should first be made in the skin, so that the needles may be passed in painlessly. Then the deeper parts should first be infiltrated, for if these layers are left till last it will be difficult to recognize anatomical landmarks through the superficial œdema. The anæsthesia lasts from one to two hours.

3 **Regional or conduction anæsthesia.**—This method of producing anæsthesia consists essentially in blocking the path of sensory impulses from a given region by injections into or around the nerves which supply it with sensation.

In a larger number of operations this perineural method is combined with infiltration, in that in the latter attempts are made to inject the drug into the neighbourhood of the nerves going to the part; but the use of pure perineural and endoneural injections has produced excellent results. The so-called spinal analgesia, considered in the next article, is of course only an extension of this method.

In making an *endoneural* injection it is necessary first to expose the nerve under infiltration anæsthesia, and then with a fine hypodermic needle to inject the solution into its substance, care being

taken not to stretch the nerve trunk tightly, and so cause considerable pain. Crile, in 1889, amputated a leg after injections of cocaine into the sciatic and anterior crural nerves, and similar operations have been done in the upper limb after injections into the brachial plexus.

The *perineural* method is best illustrated by the anæsthesia produced in the hand by injections of the solution in a ring around the wrist, especial care being taken to infiltrate the tissues around the median and ulnar nerves.

Regional anæsthesia is of great value in the upper limb. It is produced most conveniently by injecting the brachial plexus above the clavicle as it lies on the first rib at the outer side of the subclavian artery. Operations upon the thorax for empyemas, for drainage of the pleura, and the more extensive operations involving the resection of ribs and cartilages, are generally carried out under regional anæsthesia. The intercostal nerves are injected in the subcostal groove behind the angle of the rib, and a regional anæsthesia is produced which includes the whole thickness of the chest-wall and corresponds to the distribution of the injected nerve.

4. **Venous anæsthesia.**—This procedure was introduced by Bier, and is employable only on the extremities. The extremity is first rendered bloodless by the application of an elastic bandage from below upwards; this is then unwound, except for the upper two or three turns, which should lie a little above the field of operation. The part below the latter is then enveloped with another elastic bandage, so that there is a bloodless area between the two bandages. In this area a vein is selected closer to the proximal than to the distal bandage and is exposed under infiltration anæsthesia. A cannula is introduced, directed peripherally, into the vein, and 20 c.c. to 60 c.c. of a 1-per-cent. solution of novocain in isotonic salt solution is injected. As a rule, the fluid flows in with ease; but occasionally, probably from the presence of valves, it refuses to enter. After a successful injection, anæsthesia supervenes in the area between the two bandages ("direct anæsthesia") in about five minutes, and in the distal portion of the limb ("indirect anæsthesia") very soon afterwards. Bier advised that at the completion of the operation saline solution should be introduced into the vein so as to remove the drug from the part and thus prevent its sudden entry into the general circulation

On removal of the bandage, the anæsthesia disappears almost immediately; therefore it is advisable to loosen the bandage momentarily to pick up the larger vessels, and then to reapply it quickly before sensation returns, so that there may be no pain during the suturing of the wound.

The operation can, as a rule, be conducted in the area of direct

or indirect anæsthesia, and amputations through the *thigh*, *excisions* of the elbow-joint, and similar procedures have been successfully performed under anæsthesia procured by this means.

While generally applicable, this method of inducing analgesia has several disadvantages. Firstly, it may fail owing to the presence of valves hindering the entrance of the solution. Secondly, the tightly applied upper bandage is sometimes very painful; this objection, according to Momburg, may be overcome by placing another bandage directly below the proximal one as soon as the anæsthesia is complete, and then removing the first bandage. Thirdly, the rapid disappearance of the anæsthesia does not allow a completely painless finish to the operation if the wound is to be sewn up, since the reactive hyperæmia following the anæmia which has been produced gives rise *to marked hæmorrhage.* The method has not been in use sufficiently long to permit a definite opinion as to its ultimate usefulness. Local injection of drugs into arteries supplying the extremities has been tried experimentally on dogs, but has not been used on the human subject.

It is impossible here to give a complete description of the technique for the local anæsthetization of all the areas of the body by the various methods described, but it may be said that the method of local infiltration combined with an attempt to inject around the nerves going to the part is the most generally applicable. Only a few of the more important points in the anæsthetizing of the various regions need be considered.

While certain parts of the body are more or less insensitive to painful stimuli, others are especially sensitive, e g. the parietal peritoneum and the periosteum. It must be clearly understood that violent pulling or dragging always causes pain, no matter how well the area of the operation has been infiltrated, probably owing to the fact that the dragging is communicated to the non-anæsthetized tissues; therefore the operation must not be roughly performed.

Application in special cases.—While the visceral portion of the *peritoneum is insensitive to the ordinary painful stimuli,* such as pinching, cutting, etc., considerable pain and shock are caused by dragging, probably due to communication of the pull to the very sensitive parietal layer. The abdomen can always be opened painlessly under local infiltration anæsthesia. It is quite easy with a fine sharp needle to recognize the various anatomical landmarks. For instance, the anterior and posterior layers of the sheath of the rectus abdominis muscle can be defined, and the injection made right down to the peritoneum. *No doubt novocain is occasionally injected into* the peritoneal cavity when the subperitoneal tissues are being infiltrated,

but this appears to be harmless. Anæsthesia of the upper part of the abdominal wall can be obtained by injecting the lower intercostal nerves behind the lateral cutaneous branches, and a regional anæsthesia is produced which includes the whole thickness of the abdominal wall and peritoneum. The operation of gastrostomy is conveniently done with this form of anæsthesia. The peritoneum over the iliac fossa can be safely infiltrated from skin punctures about the anterior superior iliac spine, thus permitting the painless performance of appendicectomy. The disadvantage of local anæsthesia for operations involving the peritoneal cavity is that the pain due to pulling on the viscera cannot be eliminated, but even if a short period of general anæsthesia is necessary for such manipulations the advantages of the local anæsthesia for the greater part of the operation may be very great in an old and feeble patient.

An important point in the technique of local or regional anæsthesia in any situation is that the injection should be completed before the tissues are opened, because the tension under which the injection is made is a very important factor in the thorough soaking of the tissues with novocain. If the injection is made into an open wound the solution naturally follows the line of least resistance.

In the *neck*, apart from tracheotomy, which is easily performed under local infiltration, this method has been most used in enlargements of the thyroid gland. A deep infiltration is made with a fine sharp needle around the upper pole of the thyroid, special attention being paid to injections behind and in front of the sterno-mastoid muscle into the region of the cervical plexus. After these injections have been made, it will be found by experience that most of the skin area is anæsthetic; any parts which are found to be still sensitive should then be anæsthetized by local infiltration.

Circumcision is another operation which it is convenient to perform under combined local and regional anæsthesia. The injection is best made in a ring round the base of the penis, special attention being given to the loose tissues on the ventral aspect of the organ, as in this situation it is more difficult to obtain the injection under the pressure which is so essential to success.

Operations on the *skull* may be easily performed by making a ring injection around the area to be attacked; while if the infiltration is made into the pericranium it is possible to trephine the skull. It has been found that the dura mater—over the vault, at any rate—is insensitive to ordinary operative manipulations.

As far as *joints* are concerned, the cartilage-covered surfaces are normally insensitive to painful stimuli, but the ligaments and synovial membrane are not so. They can be rendered analgesic by injection of the solution into the joint cavity, so that by this measure, coupled

British surgeons. This surgeon substituted glucose for the sodium chlorid of Bier and Chaput, with the object of obtaining a solution slightly heavie than the cerebro-spinal fluid, and one which would be less hæmolytic an more nearly isotonic with that fluid. He published details of 100 cases i this year and of 200 in 1908.

Anatomical points.—1. The spinal theca extends from th foramen magnum to the second sacral vertebra.

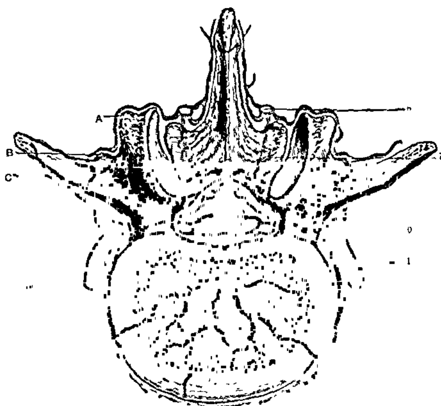


Fig. 190.—The spinal veins.

[illegible]

(From Morris's "Human Anatomy.")

2. The lowest point of the spinal cord within the theca is opposite the intervertebral disc between the first and second lumbar vertebræ.

3. The depth of the theca depends on the physical development of the patient. In the adult its average depth is 2¼ to 2¾ inches.

4. The only vessels of any importance in spinal analgesia are con-

tained in the epidural space. They are the two longitudinal venous trunks, united by transverse branches opposite the bodies of the vertebræ, with which they lie in contact, each being about 4 mm. from the middle line (Fig. 190).

5. The line joining the highest points of the crests of the ilia passes between the third and fourth lumbar vertebræ.

6. The immediate posterior relations of the theca in the middle line are, from behind forwards, the skin, the subcutaneous fat, the supraspinous ligament, the interspinous ligament, the interspace between the ligamenta subflava, and the areolar tissue of the epidural space with the veins on either side.

Characters of the cerebro-spinal fluid. (*See* p. 645.)

Indications for the employment of spinal analgesia. —This method may be used with advantage—

1. Where the operation is complicated by the presence of
   (*a*) Respiratory disease, especially bronchial and tracheal obstruction.
   (*b*) Cardiac disease, especially double mitral and aortic lesions.
   (*c*) Acute or chronic inflammation of the kidneys.
   (*d*) Aortic aneurysm.
   (*e*) Thyroid enlargement.
   (*f*) Marked atheroma.
   (*g*) Suspected status lymphaticus (possibly).

2. Where operative procedure is hampered by engorgement of the parts and consequent persistent oozing of blood, e.g.—
   (*a*) Rectal operations, with possibly the exception of hæmorrhoids, in which some engorgement is rather an advantage.
   (*b*) Prostatectomy, especially suprapubic.
   (*c*) Intravesical operations generally.

3. In operations where extreme relaxation of muscles and the absence of straining and postoperative vomiting are especially desired ·
   (*a*) Appendicectomy.
   (*b*) Colostomy.
   (*c*) Enterectomy
   (*d*) All pelvic operations.
   (*e*) All herniæ.

4. Where the operation involves great shock, e.g.
   (*a*) Double amputations.
   (*b*) Amputation at the hip-joint.
   (*c*) Acute intestinal obstruction.

Contra-indications.—Much difference of opinion exists in this branch of the subject. Many Continental writers mention old age, extreme youth, atheroma, sepsis, syphilis, gangrene, and nervous diseases as unsuitable conditions. Syphilis is no greater an objection to spinal analgesia than to other surgical procedures. As regards gangrene, the use of spinal analgesics, unless combined with some preparation of suprarenal gland, does not appear to initiate it nor promote its spread when present.

Advantages of spinal analgesia.—1. *Preoperative starvation* is neither necessary nor wise. The patient may with advantage be fed before, after, and, if necessary, during operation; the great gain to elderly and feeble subjects is obvious.

2. The *prevention of postoperative shock* is perhaps the greatest of all advantages of spinal anæsthesia. This characteristic of the method is most valuable in those cases in which severe and prolonged operations are to be undertaken on patients in comparatively good health. In cases of disease or injury where shock is already present, the preliminary fall of blood-pressure which may be occasioned by the stovaine is such as to outweigh the advantages possibly obtained by its use. This was demonstrated conclusively in the surgery of the War. Spinal anæsthesia was not of the value that had been hoped in cases of severe injury. In other words, the use of spinal anæsthesia is to avoid the onset of shock, but once shock is present the dangers of the method outweigh its advantages.

3. *Muscular relaxation* is one of the chief features of spinal anæsthesia. It is more complete than in any other form of anæsthesia, and its value is great in abdominal surgery, especially in strong, vigorous, muscular subjects. It is very valuable in the operations of prostatectomy, and it is perhaps not too much to say that some cases of large irreducible hernias could not be undertaken without its aid.

4. The *danger of sudden asphyxia* from falling back of the tongue and inhalation of vomited material *is diminished, but it should be* remembered that in using spinal anæsthesia for acute abdominal surgery, especially acute intestinal obstruction, it is by no means uncommon for the patient to become unconscious. In these circumstances measures must be taken for dealing with vomited matter as in any general anæsthesia.

5. *Nervous apprehension.*—In some patients, especially nervous women, the dread of general anæsthesia amounts to positive terror. When the fact is realized by the patient that no pain will be felt although consciousness is [illegible] the phenomena of shock, which are partly due to fear, are [illegible]

6. T[illegible] of t[illegible]d required for the establish-

ment of analgesia varies from four to ten minutes, and, as cleansing operations can be undertaken *at once*, the delay attendant upon general anæsthesia is entirely avoided. Perineal operations can always be begun in from four to five minutes.

7. *Venous engorgement, straining, and vomiting are absent.*—As there is no respiratory spasm there is no backward pressure on the venous system, consequently such operations as excision of the rectum and prostatectomy can be conducted with little loss of blood. Slight retching may be seen now and then, but it rarely lasts more than a few moments and does not endanger respiration. Straining is never seen except as the result of this retching.

8. Spinal anæsthesia is of the greatest possible value in *acute septic conditions* such as acute osteo-myelitis and appendicitis, especially in children. Patients suffering from these conditions are particularly prone to the complications of pneumonia and acidosis. It is therefore obviously an advantage to avoid a general anæsthetic.

9. *Retention of consciousness.*—This, although considered disadvantageous by some, is often a great help, for in cases in which a laparotomy has disclosed some condition unsuspected before operation, the consent to further interference can at once be obtained.

10. *The services of a special nurse can be dispensed with*, the patient being, as a rule, very well able to manage for himself on return to bed.

11. *The presence of friends immediately after operation is possible*, and, although undesirable, may yet be imperatively necessary for business reasons.

12. *In the absence of an anæsthetist*, especially in out-of-the-way parts of the world, spinal analgesia is often of the greatest service.

13. In cases where patients have unavoidably to be operated upon after a full meal, the washing out of the stomach often induces collapse: *a full stomach is no bar to spinal analgesia.*

14. *The cost of all spinal analgesics is much lower* than that of ether or chloroform. This is a very great saving in hospital practice.

Disadvantages of the method. 1. *Retention of consciousness.*—If it is seriously urged that it is undesirable the patient should see things which might frighten him, or hear remarks not intended for him, the remedy is very simple. A screen arranged as shown in Fig. 194 will overcome the first, and some damp cotton-wool in his ears the second of these objections.

2. The *special dangers* referred to later (p. 752).

3. The *uncertainty* of the method as to—

(*a*) Successful performance of injection.
(*b*) Establishment of *complete* analgesia.
(*c*) Duration of analgesia.

(*d*) Its regularity of distribution.

(*e*) Its probable height.

These questions are dealt with *later*.

4. Its unsuitability, for obvious reasons, to *gynæcological operations in the lithotomy position.*

Various agents for the induction of analgesia.—Up to the present time six substances especially have been used in this country and abroad.

1. **Cocaine** was the earliest analgesic used for intraspinal injection, but owing to its highly toxic properties it has been definitely abandoned as dangerous.

2. **Eucaine** has not survived more than a brief trial. It was found to be quite unreliable in its effects, although much less toxic than cocaine.

3. **Tropacocaine** has been much advocated by Leedham-Green, who has kindly supplied for the present article the following notes of its characters and use:—

> "It is less frequently followed (than stovaine and novocain) by unpleasant after-effects, such as headache and vomiting. The slightness of the action of tropacocaine on the motor cells lessens the possibility of the respiratory muscles being interfered with."

Leedham-Green uses 1 to 1·5 c.c. of a 5-per-cent. solution, to which he adds 3 to 9 c.c. of cerebro-spinal fluid before injection; and he draws attention to the decomposition of the drug by soda solution. He has abandoned the Trendelenburg position. The average duration of analgesia is 1·5 hours; headache is noted in 5 per cent. of cases, and shock is absent.

4. **Alypin** is a derivative of glycerin, and is neutral in reaction. It has been used abroad in combination with suprarenin borate. *It is* claimed for it that it is less toxic than cocaine, and that it produces no bad after-effects. This, however, is denied by Braun, who says it has produced "local tissue-irritation and gangrene."

5. **Stovaine** is soluble in water and slightly acid in reaction. Barker's solution, prepared by Billon of Paris, is the most convenient form, and contains 0·05 grm. of stovaine and glucose respectively *in* each c.c. This solution is non-irritating and only slightly toxic. It has perhaps been more largely used in this country than any other analgesic. It is incompatible with mercury, iodine, iodides, and alkalis.

6. **Novocain,** the most recent of the analgesics, is readily soluble in water and is neutral in reaction. It can be boiled without decomposition and is much less toxic than cocaine. It is used in 5-per-cent. solution in doses of from 2 c.c. to 3 c.c. combined with suprarenin borate, which is unnecessary and certainly inadvisable.

Preparation of patients and instruments.—No special diet is required as in the case of general anæsthesia, but where the patient is old or feeble, light nourishment should be given just before operation. It is very important that the rectum should be thoroughly cleared before operation, owing to the marked relaxation of the sphincters in spinal analgesia. The site of puncture must be *treated* just as if an operation were contemplated there, a compress being applied

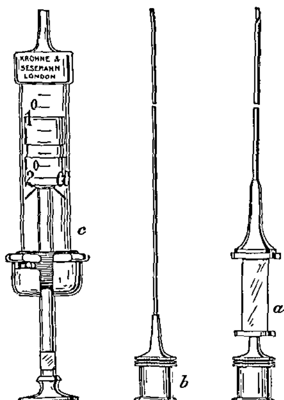


Fig. 191.—Barker's syringe and needles.

a, Hollow sharp needle containing cannula; *b*, cannula, *c*, syringe.

the night before. In urgency operations the cleansing must be very thorough, the part being treated with turpentine, ether soap, and spirit

Previous to sterilization, the needles, cannula, and syringe must be freed from all trace of grease by immersion in ether. They are then boiled in the usual way *without the use of soda or any alkali.* After use the greatest care must be taken to guard against rust, since otherwise there is every probability that on the next occasion the cannula will refuse to pass through the needles, and be bent or broken

Instruments used.—By far the best of these are the syringe and needles designed by Barker (Fig. 191). The former consists of a glass barrel in metal mounts, with a worked metal plunger, graduated to measure 2 c.c., each of the divisions being subdivided into five, and each subdivision representing 1 cg. of stovaine and 1 cg. of glucose. The needles, into the shoulder of which the nozzle of the cannula accurately fits, are 3·25 in. in length, and have their points bevelled off at rather an obtuse angle. They are fitted with stylets similarly bevelled, having a tooth which fits into a slot cut in the shoulder of the needles, to ensure the bevelled surfaces accurately corresponding. The cannula is made to pass easily through the needles and to project about 1 mm. beyond their points. The object of this may be thus explained: When the point of the needle is

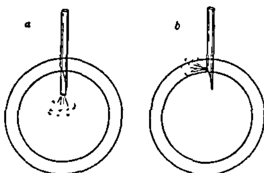


Fig. 192.—Showing (*a*) use of cannula, and (*b*) accidental loss of analgesia which it is designed to prevent.

introduced into the theca and fluid is obtained, its further advance should be arrested; it is possible at this moment for the point to be in the theca and the base of the bevelled opening in the epidural space (Fig. 192). Thus, while fluid may flow out, the analgesic may pass almost entirely into the epidural space and be lost there. If, however, the cannula be used, it acts as a director, passing into the theca and doing no damage with its blunt end; thus the *whole* of the solution may be safely lodged in the theca.

Position of the patient.—The patient may either be made to sit on the operating table, his legs hanging over the edge, and his elbows resting on his knees, the spine being thus well flexed and the spinous processes widely separated; or he may be placed upon the side of operation, his thighs well drawn up on the abdomen, and his head fully flexed upon the chest. Although the former position greatly facilitates the performance of the injection, it is not a good one: the solution tends to sink to the lower end of the theca and remain there. Further, the amount of movement required to place the patient in the supine position, after injection, appears to

affect the even flow of the solution towards the dorsal region, and this frequently interferes with the evenness and completeness of the analgesia. The lateral position, although a little more awkward for the surgeon, gives the best results.

Determination of dosage.—Only a general indication of the dosage can be given here, as much depends on the age, weight, and condition of the individual. The usual dose, however, may be taken as that which will suffice for the performance of a hernial operation in a healthy male adult. For this purpose—

The dose of tropacocaine may be 0·05 to 0·06 grm. (1 to 2 c.c. of 5-per-cent. solution).
„ „ alypin „ „ 1 to 2 c.c. of a 2-per-cent. solution.
„ „ stovaine „ „ 0·05 to 0·06 grm.
„ „ novocain „ „ 2 to 3 c.c. of a 5-per-cent. solution.

It must be remembered that patients may exhibit an idiosyncrasy for the drug; that perineal operations require the smallest, and epigastric the largest doses. It should be the rule never to give larger initial doses than are necessary.

Landmarks for injection.—The site of puncture should be strictly in the middle line of the back, any of the four lumbar interspaces being chosen, that between the second and third spines being the most convenient. According to Tuffier, a line drawn transversely between the highest points of the iliac crests crosses the fourth lumbar spine; the level of this line is liable to slight variation owing to differences in the width of the pelvis and the development of the intervertebral discs. The matter is not of importance, since the lumbar spines are easily distinguished, and any of their interspaces may be utilized. The first or second space should be chosen since, owing to the decrease in diameter of the theca towards the sacrum, the lower spaces require greater accuracy of direction in introducing the needle.

With the patient in the lateral position it is well to note the position of the spines above and below the proposed site of puncture, since there is a tendency for the spine to sag in this posture.

The injection.—The patient being in position on the table, *the head end of which is slightly lowered, or the pelvis slightly raised,* the compress is removed and the part sponged with spirit. The site of puncture being marked by the tip of the forefinger of the left hand, the needle carrying its stylet is held like a pen in the right (Fig. 193). The skin is *slightly* frozen by the ethyl chloride spray (too long an application of this is apt to turn the point of the needle), and the needle, being entered just below the spinous process above, is pushed directly forwards for about an inch and a half. The stylet is now withdrawn and the needle again pushed onwards till the appearance of fluid indicates

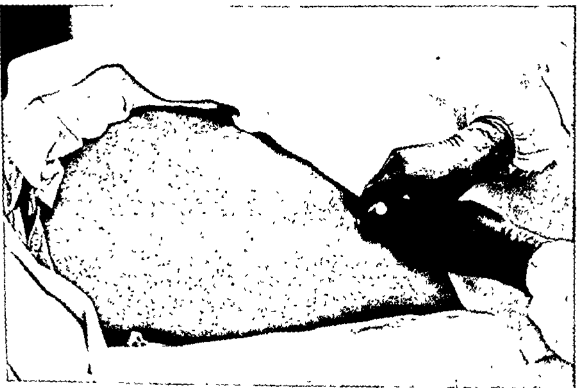


Fig. 193.—Making the injection.

that the theca has been entered: this is usually at a depth of from 2·5 to 2·75 inch. Experience soon enables one to recognize the sensation of puncturing the dura. About 5 c c. of the fluid is allowed to escape, and the cannula, mounted on the syringe, which has previously been filled to the desired dose-mark and freed from air-bubbles, is introduced into the needle up to the shoulder. The injection is gently made, and the needle and cannula are withdrawn together. It is quite unnecessary to seal the puncture wound in any way. The patient is left for a minute or so on his side, *the head being well raised*



Fig. 194.—The site of operation screened from patient's view.

on a pillow, at the end of which time he is gently rolled over on to his back, a sterilized towel being placed beneath the lumbar region. For ten minutes the head is kept well raised, so that the foramen magnum is always on a higher level than the fourth and fifth dorsal spines, which should form the lowest point of the back on the table The puncture rarely causes any pain, even when the spray is omitted. If, however, as occasionally happens, any of the cords of the cauda equina, or the periosteum of the vertebræ should be touched, pain is at once felt, and in the former case its reference to one side or other indicates the error in direction of the needle.

The flow of fluid varies greatly in its activity; and it is found that a feeble flow generally precedes a feeble and irregular analgesia.

Indications of successful injection, with relative times of occurrence.—The evidences of the solution having reached the spinal theca may, in their chronological order, be enumerated as follows:—

1. Loss of knee-jerks. At once.
2. Sensation of warmth and tingling in the feet. One minute.
3. *Loss of cremasteric and plantar reflexes.* Two minutes.
4. Numbness of feet and ankles, and analgesia of perineum, penis, scrotum, and rectum. Three to four minutes.
5. Loss of motor power in legs and analgesia to groins. Five minutes.
6. Analgesia to and often above umbilicus. Six to ten minutes.

By means of a pin-point the rise of analgesia is ascertained, and as soon as it has *attained to some distance above the site of operation* the table is levelled, or the pelvis lowered, but the *patient's head is still kept well raised for ten minutes.*

By means of a stand carrying a sheet, which passes across the chest, the site of operation is entirely screened from the patient's view (Fig. 194), and the operator can proceed.

Height of analgesia necessary for certain operations.—The analgesia passes off in an order reverse to that of its induction, and a margin must be allowed for this if the operation is to be completed painlessly. Further, this resolution proceeds comparatively rapidly, twenty minutes often sufficing to clear it from the *umbilicus to the knees; therefore analgesia should be established to* the following levels for the operations mentioned:—

Operation	*Analgesia required*
On legs	To groins.
On thighs	To umbilicus.
Genitals and rectum . . .	,, ,,
Appendicectomy	To ensiform cartilage.
Hysterectomy and pelvic operations generally	,, ,, ,,
Inguinal colostomy	,, ,, ,,
Laparotomy above umbilicus . .	To clavicles.

When the operation is nearly completed and the analgesia shows signs of resolving, it is well to begin suturing from the *top* of the wound; and here it may be mentioned that in cases of double hernia the operation should first be done on the side *opposite to that* on which the patient was lying at the time of injection, since the analgesia commonly lasts longer on the lower of the two sides.

Phenomena on the table.—In most cases the whole operation is accomplished without difficulty to the surgeon or discomfort to

the patient. *Faintness, pallor,* and *sweating,* accompanied by *slight regurgitant vomiting,* are, however, occasionally seen. These phenomena are probably toxic in origin; they usually appear in the first fifteen minutes and rarely last for more than five minutes, and after their cessation the patient remains perfectly comfortable. Compression of the abdomen seems to benefit the patient during the presence of these symptoms, but of this there is at present no proof.

In rarer cases, where the analgesia has risen to the clavicles, a sense of *chilliness and shivering,* without pyrexia, has been noted.

With high analgesia there are at times an *alteration of respiration* resembling "*air hunger,*" and *inability to cough;* there is no cyanosis or increase of respiratory rhythm, and the condition is clearly due to paresis of the intercostal muscles, the diaphragm alone carrying on respiration.

Priapism is occasionally seen, exactly as in cases of fracture of the cervical spine, but it is not always due to high analgesia. *Relaxation of the sphincters* is characteristic of the method, therefore careful evacuation of the bowels before operation, and possibly the provision of a pad of cotton-wool in the perineum when on the table, are required.

Pupillary changes have been seen, generally in the way of contraction or inequality; but they are rare and transient.

Thirst is frequently complained of, especially in association with pallor and sweating. No treatment of these latter symptoms is better than the assuaging of the former.

Duration of analgesia.—Case for case, small doses mean short analgesia, but the reverse is not always true. Nothing varies so much in this procedure as the duration of analgesia in different individuals. The average duration resulting from a dose of 6 cg. of stovaine in adults is fifty minutes, but it is at times as long as ninety or as short as twenty. As a rule, a good flow of cerebro-spinal fluid and a steady rise of analgesia means analgesia of high level and long duration. Removal of excessive amounts of fluid tends to very rapid rise and to shorter analgesia. The injection should not be made where the flow of fluid is poor. In most cases the effects of the injection will be found to have passed off in the course of from one to two hours, the knee-jerks being the last of the functions to be re-established.

Postoperative phenomena.—In this country the procedure seems to have been singularly free from unpleasant sequelæ; but on the Continent, where opinion varies greatly as regards dosage, position, technique, and class of patient, such phenomena have been reported from time to time.

The simplest sequelæ met with in ordinary circumstances are *head-*

ache, backache, pain in the limbs, sickness, and pyrexia. Pyrexia is almost always present, but the temperature rarely ranges above 101° F., and commonly subsides on the second or third day. Schwarz considers the effects to be as much due to the vehicle as to the drug, since sterilized water is of itself capable of producing such symptoms.

These sequelæ are said to be commoner where stovaine is employed, but this probably only means that that drug has been far more extensively used than any other. In the course of over 800 cases at the Seamen's Hospital, Greenwich, no serious sequelæ of any kind were met with. Many writers, however, speak of tropacocaine and novocain as being less toxic than other analgesics. The following points should be noted as making for safety:—

1. Cocaine should be entirely abandoned.
2. Pyæmia is a contra-indication to spinal analgesia, although simple sepsis is not necessarily so.
3. Preparations of suprarenal gland are probably dangerous to the *vitality of the cornual cells of the cord.*
4. Unduly high analgesia should not be purposely aimed at.

The Trendelenburg position.—The pioneer workers of *spinal anæsthesia considered that there was risk of the injected drugs* either diffusing or passing by gravity up to the medulla and so causing complete respiratory paralysis. Consequently patients were kept on the table during the operation with the head considerably raised, and also nursed in bed afterwards in the raised position. On these grounds, too, the Trendelenburg position was considered unsuitable and dangerous. Now it has been shown that the stovaine in its heavy solutions cannot be moved by gravity after a few minutes, certainly not after eight to ten minutes, and that with the lighter solutions which are now sometimes used made up in normal saline, diffusion is complete and the line of analgesia fixed in about the same time, so that it is unnecessary to keep the patient's head raised throughout the operation; moreover, it has been shown to be a disadvantage, tending to lower the blood-pressure and so increase the risk of pallor, sweating and vomiting. It is even permissible to go a little further and use a slight Trendelenburg position even where the operation does not require it in order to keep up the blood-pressure. Spinal anæsthesia is now extensively used for long operations, such as Wertheims hysterectomy and excision of the rectum, in which operations the prevention of shock and muscular relaxation are so valuable. The only disadvantage of the extreme Trendelenburg position is the discomfort to the conscious patient, so that a little general anæsthesia or scopolamine and morphia are generally used for psychic reasons Any danger that there may be in the Trendelenburg position is not associated with respiratory paralysis, but is due to the weight of the

abdominal viscera pressing upon the heart and lungs. This may be serious in a fat patient, so that the Trendelenburg position should always be attained very gradually, and the steepness of the slope diminished at any time if necessary.

Causes of failure to enter the spinal theca.—1. The spines may be very closely set; the vertebral column may be osteo-arthritic or the seat of an old injury.

2. The theca may be of very small diameter, tough, or thickened by old pachymeningitis.

3. The needle-point may be blunt, or may be turned by encountering bone during its passage, and so may push the theca before it *without perforating it.*

4. Inaccuracy of direction may carry the needle to one side or other; this may easily happen if the patient's body is twisted on the table.

5. In very stout patients, in whom the bony landmarks are absent, accurate judgment is necessarily replaced by pure guesswork.

Causes of failure to get a good flow of cerebro-spinal fluid.—1. In old and wasted patients deficiency of fluid may be the cause.

2. In some cases failure is probably due to the rush of fluid carrying a nerve cord, or a fold of arachnoid, against the orifice of the needle; this difficulty can often be got over by rotating the latter so that the orifice faces in a different direction.

3. The theca, instead of being punctured in the centre, may be entered at one side; or the needle, if passed too rapidly with the stylet in place, may traverse the theca and emerge on the anterior surface. In such cases a very small quantity of fluid may pass out of the needle, but as soon as the cannula is inserted its orifice will be blocked, or its point will pass out of the theca and the solution be lost in the epidural space.

4. Occasionally a small vessel may be opened in the tissues of the back, and the needle become blocked with clot. This is likely to happen when a failure to find the theca in one direction is followed by a second attempt in another without entirely withdrawing and clearing the needle.

Cause of failure to get satisfactory analgesia.—Provided the flow of cerebro-spinal fluid has been active, the drug fresh and uncontaminated by contact with incompatibles, and the injection properly conducted, insufficient analgesia is always the result of insufficient dosage.

Mechanical aids to sluggish rise.—Where the analgesia lags after injection, the solution can be induced to rise in the theca by either of two methods.

1. The intraventricular pressure in the brain may be diminished by causing the patient to take three or four sudden and deep inspirations, thus causing a partial vacuum which must be met by a slight upward flow of the thecal contents. This will only assist to a trifling extent.

2. The force of gravity may be utilized by increasing the declination of the head end of the table. This may help if done within the first ten minutes or so from the time of injection.

Second injections.—There is no objection to a second or even a third injection, if necessary, provided the practice is carefully safeguarded. The points to be considered are (1) the age of the patient, (2) his condition on the table, (3) the amount of the original dose, (4) *the time which has elapsed since the first injection, and* (5) *the* probable duration of the operation.

If after injection *no* analgesia results it is certain that none of the solution has entered the theca. The original dose may then be repeated.

In young subjects it is well to use only one-third the original dose, since it is found that in them second doses are more rapidly effectual than in adults, and, case for case, produce a more rapid and higher rise on a proportionately smaller dose.

In the case of adults, in whom the ordinary dose is 6 cg. (stovaine), insufficient rise from the first may be met by an additional dose of half the original quantity. If some time has elapsed since the initial injection and the patient shows no toxic symptoms, the dose may be two-thirds the original amount. If the analgesia is no higher than the groins, the original amount may be repeated with safety. Each case must be judged on its merits.

The needle and cannula must never be left *in situ* to provide against a second injection; the practice, although advocated by some surgeons, is as needless as it is dangerous. It is easy to cover the wound, roll the patient over, and give a second injection during operation.

Use of general anæsthesia with spinal analgesia.—It may happen that towards the end of an operation, especially in abdominal section, some dragging pain, or the insertion of sutures, may be felt. In such cases it may be hardly worth while to repeat the *injection, and the difficulty may be met* by the administration of a very small quantity of a general anæsthetic. Spinal analgesia is no contra-indication to this, and a very much smaller amount of ether or chloroform will be required than would otherwise be the case.

Possible dangers of spinal analgesia.—Experience goes to show that these arise very rarely. They are :—

1. **Septic meningitis.**—This must come first on the list because when it occurs the condition is hopeless. With ordinary care it should never be seen. *Almost the only recorded cases are those occurring*

in the presence of already-established pyæmia, which, as stated, is a contra-indication to the method.

2. **Injury to the cauda equina.**—Although few complaints are made by patients of the pain which points to this accident, it must be admitted that contact with the needle does from time to time occur. Provided that the puncture is gently performed, little damage can result; and even were one of the nerves to be pierced, this would still probably be so, since Crile's practice of injecting nerve trunks as a protection against shock is not followed by any ill effects.

3. **Injury to the spinal cord.**—This could only happen as the result of injection above the first lumbar spine. With reasonable care and a fine needle there is little probability of any damage being done, even where high injections are made. The slightest contact with the cord would at once be felt. It is doubtful even if a slight puncture would injure the cord.

4. **Hæmorrhage into the spinal canal.**—This accident is improbable, and experience shows it to be extremely rare

5. **Persistence of paresis or paræsthesia.**—This is also rare, but it is quite possible where preparations of suprarenal gland are used. It can only be due to pathological changes in the cornual cells or in the nerve roots. As an *immediate* consequence of the injection it might be attributed to the former, but if occurring at a later date and involving only the distribution of one nerve or part of a nerve, it suggests fibrosis from puncture of that nerve; or in the case of monoplegia or paraplegia, hæmorrhage into the spinal canal or theca.

6. **Lasting retention of urine and incontinence of fæces.**—Little is known of these complications, no sufficiently authenticated case having been reported

7. **Toxæmia.**—The various analgesics differ in their degree of toxicity, and the depth of the toxæmia is not entirely due to the amount of the drug used. Some patients undoubtedly exhibit idiosyncrasy to some of them, even in comparatively small doses insufficient to produce high analgesia; and this must be remembered in dealing with children.

8. **Asphyxia.**—This is, of course, the direct result of high analgesia. Even after the table has been levelled in order to limit the further ascent of the solution in the theca, the analgesia will at times attain a slightly higher level, owing probably to the diffusion of the drug. A close watch must therefore be kept on this rise as it approaches the second or third dorsal nerve-area. At this height it is clear that the intercostal muscles must be paralysed and the diaphragm alone left to carry on respiration. Especially must the rise due to forced inspiratory efforts in bronchitic and asthmatic subjects be remembered and allowance made for it.

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These cases were all done with stovaine, and, seeing that at least six of them were satisfactory so far as respiration is concerned, it is possible that some safer drug may be found which will overcome the difficulty of respiratory paralysis.

Spinal analgesia in children.—The statement that this method is contra-indicated in children was shown to be unfounded by the work of Tyrrell Gray. *The ages ranged from 3 months to* 13 years. In the earlier cases Barker's stovaine-glucose solution was used, but in the later a solution of stovaine and dextrine, which apparently tends to diminish the amount and rate of absorption of the stovaine into the circulation, and thus some of the unpleasant sequelæ, and to give greater accuracy of localization. I (L. McG.) use the interval between the 3rd and 4th lumbar spines for puncture. The results have been excellent, especially in the case of operations for intussusception, the mortality of which has been appreciably lowered.

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TUBERCULOSIS

By J. M. BEATTIE, M.A., M.D.

This infective disease, resulting from the invasion of the tissues by *B. tuberculosis*, is met with as a local and as a general affection.

The local conditions are those which specially concern the surgeon; but the general condition is also of importance, especially in its relations with the local affection. The two are not infrequently associated with one another, and a general and widespread infection may be secondary to, and may be the cause of death in, a local form of the disease.

The causal organism can generally be demonstrated, at one time or another, in the various foci of the disease. It may be present in very large numbers, or it may be so scanty that microscopical examination fails to detect it. Inoculation results are always positive if the bacillus is present and in an active condition.

There seems now no reason to doubt that the disease in the human subject may be caused by either the human or the bovine bacillus, and experimental evidence proves that many of the lower animals may be infected with either form of the bacillus.

Methods of infection.—Ingestion of tuberculous material is no doubt a fruitful source of infection. Meat, milk, and other articles of diet may contain *B. tuberculosis*. The bacilli may be arrested on the tonsils or on other lymphatic tissue in this region, but they also pass through the stomach and become lodged in the intestines, or pass directly through the intestinal wall by the lymphatic channels and so reach the mesenteric glands In the intestines no evidence of any primary lesion may be found, but in many cases, especially in older children and in adults, proliferative and ulcerative changes are present. The mesenteric glands become swollen and show proliferative changes, caseation, etc., producing the condition of tabes mesenterica. Tuberculous enlargement of the glands in the neighbourhood of the cæcum, which is occasionally met with in young adults, appears to be due to a primary infection of the cæcum or to the passage through the cæcum of the bacilli without direct infection of its wall.

Much importance has been attached by Calmette and others to infection by way of the alimentary canal, but, though it must be

given an important place, I do not think it is the commonest channel by which the bacilli reach the tissues in the human subject.

In the infected mesenteric glands, particularly in young children, the bacillus characteristic of *bovine tuberculosis is frequently found* to be the causal agent.

Intestinal tuberculosis may also occur as the result of the swallowing of sputum by patients suffering from the pulmonary form of the disease.

Inhalation *of dried bacilli*, derived from any source—e.g. the dried sputum of tuberculous patients—or *inhalation of fine, moist* sprays which have become infected by means of sputum or in other ways, is probably the commonest method of infection. The bacilli pass directly to the trachea, larger bronchi, or lungs, where they settle down and produce their characteristic changes; or they become *arrested on the moist surfaces of the tonsils or the adenoid tissue of* the naso-pharynx, and from these situations pass to the neighbouring glands. The tuberculous cervical lymphatic glands, which are so common in the practice of every surgeon, are in the majority of cases infected from the tonsils or adenoid tissue of the naso-pharynx. This *emphasizes the importance of surgical attention to enlarged tonsils* and to adenoids. *As already stated, bacilli are also arrested in these situations during the ingestion of infected food material.*

Infection by means of **abrasions or wounds of the skin** is not common, though post-mortem warts and, it may be, lupus vulgaris arise in this way. *Occasionally surgical wounds have accidentally become contaminated with B. tuberculosis*, and tuberculous lesions have been produced. Wounds made with material previously infected with the bacillus, if not very thoroughly cleansed, may be the starting-point of definite tuberculosis. Several cases have been recorded, such as that of Tscherning of Copenhagen, where *a finger had to be amputated and glands in the elbow* and axilla excised in a woman who had cut her finger with a broken glass vessel containing the sputum of a phthisical patient.

Obscure methods of infection.—The method of infection in a certain proportion of cases, *especially those occurring in bone and in the brain*, is not at all clear. In some there is probably a spread, by way of the lymphatics, from infected lymphatic glands; but in other cases, and particularly in localized tuberculous affections of the bones and the joints and of the testicle, a carriage of the *bacilli by the blood-stream seems the only reasonable explanation*. In such cases, *too*, there is often a local cause determining the site of attack—e.g. a previous injury, or a non-tuberculous inflammatory focus.

Infection of an infant from its mother is brought about through one or other of the ordinary channels, and *by the ordinary*

methods, of which inhalation of tuberculosis sputum and ingestion of tuberculous milk are the commonest. Direct transmission of the tubercle bacilli from the mother to the child by way of the placenta may take place. So-called "hereditary transmission" I cannot regard as anything more than an inherited *predisposition*—a natural weakness which renders the infant more liable to attack.

The **extension of local tuberculosis** in the body may take place in several ways. There may be a direct infiltration of the surrounding tissues, as is seen in superficial tuberculous infections of the skin; passage to various parts by way of the lymphatics, even in a direction opposite to that of the lymph-stream; extension along air or other natural passages; and direct transmission by the blood-stream. Thus, tuberculosis of the air-passages is often found in association with tuberculous disease of the lungs, the former being caused by the infected sputum lying constantly in contact with their mucous membranes.

The spread along natural passages is very well illustrated in cases of genito-urinary tuberculosis, where the disease, starting in the testicle, may extend along the whole length of the vas deferens to the vesiculæ seminales and the urinary bladder, or even up the ureters to the kidney.

Tuberculosis of the pleura, pericardium, or peritoneum may become widespread in these membranes, merely by the bacilli coming in direct contact with them; or the condition may be more localized in the membranes, and the neighbouring lymphatic glands may become specially involved by the passage of the bacilli along the lymphatic channels.

Spread by the blood-stream is less common, and is generally due to ulceration of a tuberculous focus into an artery or a vein.

Effects produced by the introduction of B. tuberculosis or material containing it into susceptible animals.—Into whatever tissue the bacilli are introduced, the resulting changes are practically identical, and therefore a study of the condition in one tissue—e.g. the peritoneum—will be sufficient to illustrate the microscopical characters of a tuberculous lesion.

After the introduction of the bacilli there is a preliminary polymorphonuclear leucocytosis, which in about two days is followed by a great increase in the mononucleated cells. These cells are the main formed constituent of the exudate after the fourth or fifth day. They ingest large numbers of the bacilli, and persist till the death of the animal. Examination of the omentum shows the bacilli lodged at various points; and at these foci, even in twenty-four hours, mitosis and proliferation of the fixed connective-tissue and endothelial cells are seen. The proliferation increases, and in from

three to five days the bacilli become surrounded by a definite zone of these cells, which are rounded or oval in shape, have a vesicular nucleus and abundant cytoplasm. These **epithelioid cells** (Plate 66, Fig. 1) are almost certainly derived by a proliferation of the endothelial cells lining, especially, lymph spaces and channels *at the focus of infection*, and probably also by an actual multiplication of the fixed connective-tissue cells. In these cells the bacilli are found in great numbers, *often so numerous as to suggest a local multiplication within the* cytoplasm.

In from six to ten days these local areas of epithelioid cells become surrounded by a zone of small round cells with all the characteristics of lymphocytes (Plate 66, Fig. 1), and constitute the **tubercle follicle.** The lymphoid cells are derived partly from the local fixed cells by proliferation, but many of them migrate to the focus from the lymph- and the blood-vessels, the peripheral blood at this stage showing a distinct lymphocytosis

Transitions between these lymphoid cells and the epithelioid cells can be made out, and it is possible that those lymphoid cells which *are derived from the fixed connective-tissue cells may be capable of* becoming epithelioid cells, though on this point there is some doubt.

The relative numbers of epithelioid and lymphoid cells vary considerably in different cases, and also in different areas in the same case, and this variation does not appear to be due to the age of the nodule. Some early nodules may show only epithelioid cells, whilst in others the lymphoid cells may be very numerous and may partially obscure the epithelioid elements.

In from eleven to fifteen days after the inoculation the central parts of the nodules undergo **caseation.** The outlines of the central cells become indefinite (Plate 66, Fig. 2), the cells seem to coalesce, and the nuclei lose their staining reactions. Thus is produced a central, granular, or structureless area, surrounded by a more or less definite zone of lymphoid cells. With the increase in size of the nodules the *area of caseation becomes more marked.* Separate foci coalesce, and thus large caseous nodules are produced.

In certain of these nodules, especially in those slowly produced, characteristic **giant cells** *are observed (Plate 67, Fig. 1).* These are irregular masses of cytoplasm, having a granular appearance, due to caseation, and containing numerous nuclei, either arranged at the periphery or *more irregularly scattered in the body of the cell. Various* views have been put forward as to the origin of these cells, but all recent work seems to indicate that they are formed either by a fusion of the epithelioid cells or by a multiplication of the nuclei *of these cells* without a corresponding division of the cytoplasm. In the central caseous part of the nodules and in the giant cells the *B. tuberculosis*

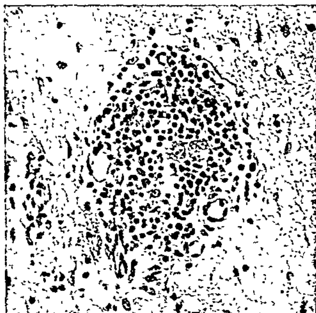


Fig. 1.—Early tubercle nodule from knee-joint, showing epithelioid cells and lymphocytes. × 300.



Fig. 2.—Early tubercle nodule from the omentum, showing loss of outline of central epithelioid cells (caseation). × 200.

PLATE 66.

(From Beattie and Dickson's "General Pathology.")

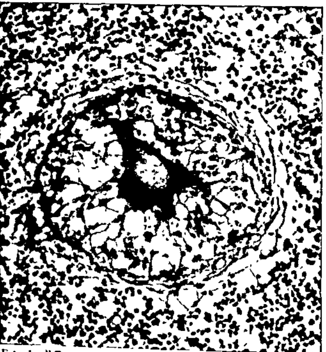


FIG 1.—"Giant-celled system," showing giant cell with central caseation, fibrous trabeculæ, and zone of lymphoid cells. × 200

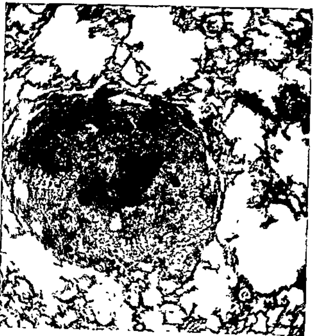


FIG 2.—Nodule in chronic tuberculosis of the lung, showing central caseation, giant-cell formation, and peripheral fibrous-tissue overgrowth. × 50.

(From Beattie and Dickson's "General Pathology.")

PLATE 67.

may generally be found, the caseation being largely due to the local action on the tissues of the products of the bacillary activity. During the process of the formation of the tubercle follicles the endothelium of the vessels at the focus becomes swollen and undergoes degenerative changes, and as a result occlusion of the vessels is brought about. Thus the nodules are non-vascular, and this absence of vessels is no doubt one of the causes of the central degenerative changes.

The caseous parts may undergo softening and liquefaction, and thus irregular cavities or ulcers may be produced.

In chronic cases an **overgrowth of fibrous tissue** (Plate 67, Fig. 2) takes place. This may occur especially at the periphery of the nodule, and thus the caseous area may become enclosed in a fibrous capsule. Commonly, however, the fibrous tissue extends inwards towards the centre of the nodule, and processes may be found in direct communication with the periphery of the giant cells, or it may also extend at the periphery and invade the surrounding tissue. In this way the *B. tuberculosis* may be completely shut in, and with the overgrowth of fibrous tissue a complete healing of the nodule be effected. It is usual, however, to find a certain amount of caseous or calcareous material towards the centre of even extremely dense fibrous scars which have originated as a result of infection with the *B. tuberculosis*, and, microscopically, giant cells are frequently seen.

Naked-eye appearances of tubercle.—The nodules are at first small, rounded, or irregular in shape, translucent or grey in colour, and firm in consistence. These "grey granulations" may be few in number or may be widely scattered and extremely numerous—*miliary tuberculosis*. They gradually increase in size, separate nodules coalesce, and thus larger caseous areas are produced. The nodules are commonly surrounded by a zone of hyperæmia, and there may be distinct inflammatory reaction. It is not uncommon in tuberculosis of serous membranes to find the nodules embedded in a thin layer of lymph, and the cavity lined by the membrane may contain an excess of turbid fluid. In some situations the nodule may be surrounded by a definite zone of granulation tissue.

In certain cases, instead of forming discrete nodules, the tuberculous process is seen as a general infiltration from one focus. Thus, extensive infiltration of the testicle may be the result of a local spread from a primary centre in the epididymis; or, again, localized tuberculous masses in the brain, and especially in the cerebellum, generally arise in this way.

As these masses increase in size they undergo degenerative changes, especially of the nature of caseation, and they assume a yellowish-white colour. These "yellow tubercles" may form nodules from one to two inches in diameter, which may become encapsuled by

dense fibrous tissue, may undergo softening or liquefaction, or may become calcified. Softening and breaking down are especially seen in infections of the skin, testicle, kidney, and synovial membranes, and are also common in the lymphatic glandular infections, whereas *calcification* and *fibrosis* are more common in lymphatic glands than in other situations.

Tuberculous abscess.—This form of chronic abscess is due to a breaking-down of tuberculous caseous material into a thick creamy fluid, but is always accompanied by more or less inflammation of the surrounding parts. The wall of the abscess may be lined by caseous material, or it may be made up of condensed fibrous tissue. This subject is dealt with more fully at p. 218.

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ACQUIRED SYPHILIS

By Brevet-Colonel L. W. HARRISON, D.S.O., K.H.P., R.A.M.C. (Ret.)

Definition.—A disease due to invasion of the tissues by a specific organism variously termed *Spironema pallidum*, *Spirochæte pallida*, and *Treponema pallidum*.

Course and main clinical features.—The virus is contained in the exudate of syphilitic lesions, and possibly in semen, and infection is usually conveyed by sexual intercourse to some part of the external genitals or of the vagina or cervix. Any other part of the external surface of the body, the interior of the mouth, nose and pharynx, or the anal canal may, however, be the site of inoculation After an *incubation period* which ranges from nine to ninety days and averages about thirty, a *papule* appears at each site of inoculation, and grows in a few weeks to a size varying from that of a lentil to that of a shilling, usually becoming somewhat eroded in the centre but not often severely ulcerated. The tissues surrounding the erosion become indurated to a varying degree, appreciable by palpation. After some weeks the initial sore gradually retrogresses, a process which is considerably hastened by treatment. In very rare cases no initial sore has appeared (*syphilis d'emblée*). These have chiefly been instances of accidental inoculation by a surgical needle.

A few days after the appearance of the initial lesion the neighbouring *glands* usually become painlessly *enlarged*, and this is followed by enlargement of palpable glands throughout the body, notably the epitrochlear, axillary, and cervical glands.

When the primary sore has appeared the *blood-serum*, as a general rule, gradually acquires a peculiar property demonstrated by the Wassermann test. This property is present in over 50 per cent of cases by about the fifteenth day, and in practically 100 per cent. by about the thirtieth. About a month or six weeks after the appearance of the sore, and often while this is still present, a measles-like *rash* appears on the trunk and spreads gradually to the limbs and face. The soft palate is usually erythematous. The patient may at this time feel mildly feverish and suffer from headache and malaise. There may also be a certain amount of *secondary anæmia*, which in

rare cases is very severe. A few weeks later a *papular eruption* appears on the trunk, limbs, and face, and generally in the same order of distribution. The *papules* vary in appearance in different sites, and are often confluent and prominent between the buttocks, between the scrotum and thighs, and on the labia, constituting wart-like growths called *condylomata lata*. The papules themselves are always more or less scaly (papular, papulo-squamous, and squamous syphilides). Uncommonly they necrose and become pustular to a varying degree (papulo-pustular and pustular syphilides). *In the mouth and throat* the eruption is usually represented by confluent papules with eroded or macerated centres called *mucous patches*. At this time, or somewhat later, the *eye* may be invaded, and iritis or choroiditis result. The rash recedes in the course of some weeks, and the next event, after months, perhaps, have elapsed, may be a series of more ulcerative lesions with scabbing—superficial and deep *ecthymatous syphilides*, both of which are very uncommon.

The usual event following the papular eruption is a *period of quiescence*, which may last the remainder of the patient's life or be interrupted after anything from one to fifty years by a recurrence in the form of a single lesion or a few lesions occurring at spots which have received some more or less trivial damage by trauma or strain Any part of the body framework, generative organs, viscera, or central nervous system may be the site of these late or *tertiary lesions*, and their size, character, and seriousness depend largely on the site of the recurrence. Generally they consist of granulomata which tend to necrose in the centre and become fibrotic at the margin, and to interfere seriously with the function of the tissue affected.

Besides the above gross lesions, certain other manifestations may be mentioned, though they concern the physician rather than the surgeon. From the stage of the secondary rash, or even before it, syphilitic meningitis, meningo-myelitis, myelitis, and meningo-encephalitis may occur and lead to various forms of paralysis. The invasion of vessels, which occurs early, is manifested at a much later stage by aortitis, with resulting aneurysm or aortic regurgitation, by myocarditis, and by aneurysm of such vessels as the subclavian, carotid, femoral, and popliteal arteries. The parenchyma of the liver or kidneys may suffer early, and acute yellow atrophy and acute nephritis are met with, though very uncommonly, in the so-called secondary stage. Degeneration of the parenchyma of the central nervous system in the form of general paresis and tabes dorsalis may occur as late events, usually after the fifth year.

It must be remembered that any or all of the manifestations outlined above may be omitted, and very occasionally, as mentioned, even the primary sore may not appear.

varieties of this organism are finer and much shorter than an average specimen of *Sp. pallidum*; one variety has much closer-set coils, which seem almost to touch, and in the other the coils are angular.

Resistance to external agencies.—*Sp. pallidum* is killed at once by drying, by comparatively low temperatures (probably ordinary hot water for washing up dishes kills it), and by much feebler antiseptics than suffice to destroy, for example, *B. typhosus*. The organism was first cultivated by Noguchi, and seems to be an obligatory anaerobe

Pathology.—After entering an abrasion—one of the slightest degree being sufficient for infection of man—*Sp. pallidum* remains fairly close to the surface, where it can be reached by antiseptics, for certainly an hour and possibly for four to six hours. After this it is usually beyond reach, having penetrated to the deeper parts, from which it quickly invades the tissues of the body generally. The route is probably almost always at first along lymph channels, including perivascular and perineural lymph spaces. There is evidence that, even in animals (which are more resistant than human beings), the spleen, testes, and bone-marrow are invaded within a few days of inoculation; and, long before *Sp. pallidum* was discovered, men accidentally killed during the early days of the primary sore were found to have syphilitic changes in the retroperitoneal, mediastinal, and other glands throughout the body. After the incubation period a lesion appears at the site of inoculation. Syphilis has been divided in the past into stages—primary, secondary, and tertiary—mainly because of the period of quiescence which succeeds each recrudescence, and because the succeeding manifestations differ in clinical characters from their predecessors. But histologically the syphilitic lesion affecting supporting and nutritional structures of the body and its viscera, which are those usually affected, is essentially the same. A study of the histology affords an insight into the reason of many of the features of syphilis The reaction of the tissues to the stimulus of the syphilitic virus is very similar to that seen in tuberculosis: a proliferation of the connective-tissue and endothelial cells, with an increase of lymphocytes and plasma cells, constituting an infective granuloma, which differs from the granuloma of tubercle largely in the absence or scantiness of giant cells, and in the smaller tendency to liquefactive necrosis and calcification. An important part of the process is seen in the small blood-vessels, around which, indeed, the process is most intense. The plasma and endothelial cells are heaped up in the perivascular lymph space, and the outer and middle coats of the vessel become the seat of accumulations of cells which here and there interrupt the muscular and elastic layers. The internal coat becomes thickened (endarteritis obliterans), interfering with or

completely interrupting the flow of blood through the vessel. Ultimately the cell accumulations are converted into fibrous tissue, so that the arterial wall becomes thickened and hardened in patches. Rarely true gummata form in the walls of large arteries, and may break down.

The lymphatics draining a syphilitic granuloma become infiltrated, and the parts distal to the lesion undergo a lymphatic œdema which is well seen in the œdema of the prepuce and meatus and of the labia when primary sores sit astride the lymphatics draining these parts (*syphilitic indurative œdema*). Though the histological process is qualitatively the same in its inception in all stages of syphilis, the degree of change varies considerably, and this is no doubt due to the alteration in the reactive power of the tissues, which becomes greater and greater as the infection becomes older. In the beginning, judging by the large numbers of spironemes to be found in a primary lesion, the tissues are slow to react. Though the primary lesion may eventually reach a fairly large size, about that of a sixpence or a shilling, it seems to have done so in response to the stimulus of a very large amount of virus. In the early roseolar stage it is difficult to judge the number of spironemes, because they are less accessible, but in stages later than the early roseolar the lesions tend to become larger though scantier, and *Sp. pallidum* to be less and less numerous in them. In the so-called tertiary stages a long search is usually necessary to discover even a few spironemes

The ultimate fate of a syphilitic lesion depends on a number of factors. There is the accumulation of cells which would become fibrous tissue if natural processes did not tend to their removal, or if the action of the virus and the local arteritis and occlusion of vessels, interfering with their nutrition, did not tend to result in their necrosis. In the primary stage the usual result is either complete removal or a varying degree of fibrosis which may become cartilaginous in consistence. This fibrosis is particularly apt to occur in sores affecting the mucous surface of the prepuce, and is less common in the skin, the glans penis, and the anterior commissure of the female genitals. The shrinking of the scar often leaves a characteristic dimple in the centre The vascular infection is doubtless responsible for the oozing of blood into the lesion which is well seen in chancres of the coronal sulcus and those of the skin, the latter being often covered by a black scab. Necrosis is not a prominent feature of primary sores, and is usually very superficial unless the lesion becomes a prey to secondary infection, when the part sometimes becomes phagedænic and destruction of tissue is rapid and severe.

An important result of the fibrosis of primary sores, and also probably of occlusion of vessels feeding the centre, is that spironemes may be

buried there, safe from attack by remedies circulating in the blood. Many weeks, months, or years later these may re-awake and the old lesion break down, resulting in a recurrent chancre or in a chanciform gumma, the former being not only the earlier, but clinically more like a chancre than a gumma, while the latter is the reverse. The earlier roseola seems to resolve completely. The secondary papules of the skin, the *condylomata found between the buttocks*, and the prominent frambœsiform lesions sometimes seen on the face, are considerably slower in resolution than the early roseola and the lesions of mucous membrane, but ultimately resolution appears in most cases to be complete. Papular lesions show evidence of interference with the nutrition of their central and superficial parts in the varying amount of scaling which characterizes all of them. In some cases the centre of the papule necroses (papulo-pustular syphilide); in others, comparatively rare, the whole papule breaks down to a pustule (pustular syphilide).

In the later, so-called tertiary stages of syphilis, fibrosis, or ulceration, or both are practically always found. Why in one tertiary lesion the process never results in ulceration but always in scarring, why, in another, ulceration is a prominent feature, and why, in still another, fibrosis is pronounced at the edges and ulceration in the centre of the lesion, is not definitely known Probably the outcome depends on a number of factors. The general health of the patient is important, lesions in the ill-nourished tending more to ulceration. The size of *the lesion determines the distance from the open vessels at the periphery* to the centre, and a large granuloma is more likely to break down in the centre than a small one. Similarly, the general blood supply of the part must affect the liability to necrosis. In the periphery of a tertiary lesion there is usually considerable hyperplasia, *resulting in* sclerosis, which is appreciable in all tertiary lesions but perhaps is most emphatic in the ivory-like ring of sclerosed bone surrounding *a gumma of bone.*

The changes resulting from disease of arteries supplying important organs such as the heart, brain, and spinal cord, as also the changes resulting from direct poisoning of the parenchyma of the liver, brain, and spinal cord, belong properly to a work on medicine and cannot be described here.

Laboratory aids to diagnosis. Microscopical examination.—The discovery of *Sp. pallidum* by Schaudinn at once placed in our hands a most valuable aid to diagnosis in the microscopical examination of secretion from all the earlier, including secondary, types of syphilitic lesion. The method of choice, by dark-ground illumination, is one which, after a very little practice, becomes extremely simple; so much so that it falls within the *province of the clinician*

rather than of the pathologist, and a microscope fitted with a dark-ground condenser is a necessary part of the armamentarium of everyone who has to examine patients suffering from syphilis. The method of obtaining the secretion will be detailed under each of the types of lesion to which microscopical examination is applicable; here it may suffice to indicate the chief steps of setting up the specimen for examination.

The microscope is fitted with a special type of substage condenser, which is slipped into the place of the ordinary condenser when dark-ground illumination is required. The usual objective employed is a $\frac{1}{12}$-in. oil immersion fitted with a stop which can easily be removed when the lens is required for ordinary work. The oculars are the ordinary ones supplied with a bacteriological microscope. The slide is of the thickness recommended by the maker of the dark-ground condenser; the coverslip is of the ordinary, thin variety. A strong illuminant is necessary, such as a "Pointolite" (for direct current only), a carbon electrode arc with electrodes set at right angles, or a substage illuminator made for dark-ground work. Either of the arc lamps requires a bullseye condenser to direct parallel rays on to the plane mirror of the microscope. The steps of the examination are as follows:—

1 Place the drop of secretion on the slide and cover it with the coverslip, causing as few bubbles as possible.

2 Turn the slide over, coverslip down, and press it firmly on a few thicknesses of filter paper, to make the specimen as thin as possible.

3 Rack up the condenser till it is flush with the microscope stage, and then examine the top of it through the microscope, using a low magnification such as $\frac{2}{3}$ in objective and No. 2 eyepiece. Two rings engraved on the top of the condenser should be seen and worked to the middle of the field by means of the centring screws on the condenser.

4. Rack down the condenser slightly, put a drop of oil on the top of it, another on the under surface of the slide, opposite the specimen, and place the slide on the stage. Rack up the condenser till it is again flush with the stage In the result there should be no air-bubble in the oil between slide and condenser, if there is, the operation must be repeated.

5 The light being condensed on the mirror and reflected by the latter

Wassermann reaction—This test is an application to syphilis of the Bordet-Gengou method of detecting infection with specific microbes by the fixation of complement. It was announced by Wassermann, Neisser, and Bruck in 1907, and although it has since

been found *not to depend on the presence in the blood-serum of antibody to Sp. pallidum*, as was thought at first, it has proved to be *one of the most practicable and reliable of all laboratory aids to* diagnosis and one which is universally applied.

The test is described in detail elsewhere (p. 53). A negative result is indicated by the red cells becoming laked and the mixture becoming transparent like red ink, and a positive by their remaining intact, the mixture remaining turbid until the cells sink to the bottom of the test-tube, leaving a watery-looking fluid above.

The complexity of the test lies in the grading of the proportions of the ingredients, since it is possible to make a normal serum give *a positive reaction, and a syphilitic serum a negative. A matter of* great importance and some regret is that laboratory workers should differ so widely in their methods of conducting this test—in their preparation and the relative proportions of the ingredients, and in their standards of what constitute positive and negative reactions, so that, with weakly acting serums, some pathologists will return positive reactions, others doubtful, and yet others negative. Owing to the complexity of each of the various ingredients, and to the fact that a pathologist usually thinks his own method as good as any and better than most, uniformity of technique is unattainable. The important point for the clinician is to learn to understand his pathologist. He cannot do better than watch the percentage of untreated secondary cases returned as positive (it should be almost 100), and the percentage of negative results after treatment, say after seven injections (totalling 4·2 grm.) of "914": if it is a very high one in these days the test may easily be leaning unduly to the negative side. He should consult with the pathologist over the concordance, or otherwise, of clinical and serum findings, and if the pathologist is wise he will adjust his standards to attain the highest possible percentage of legitimate positive reactions.

Precipitation or flocculation tests.—*Recently the serum test* by which the addition of a syphilitic patient's serum to a diluted heart extract results in a flocculation of the mixture has been greatly improved. The most notable of the modern precipitation tests are the Sachs-Georgi, Meinicke, "Sigma" (of Dreyer and Ward, p. 56) and Vernes tests. None of them has yet supplanted the Wassermann test, but they now offer a hope of doing so, and if this happens the prospect of securing uniformity of technique will be greatly *improved.*

Use of the Wassermann test in diagnosis. The negative reaction.—There is no stage of active syphilis in which a negative reaction does not occur, so that it can never by itself exclude syphilis. In the early primary stage it is the rule; when the sore is about

fifteen days old, about 50 per cent. give a negative reaction; and about the time of outbreak of the secondary rash the percentage of negative reactions obtained by the most delicate tests is less than one. In later stages negative reactions are seen rather more frequently than in the secondary A point of practical importance is that a small dose of an antisyphilitic remedy ("provocative injection") may convert a negative reaction in a syphilitic subject into a positive, this is made use of in diagnosis, though if the reaction remains negative after a provocative injection the fact does not exclude syphilis. In a primary case, if the reaction is still negative, it is a fair inference that the disease has not advanced so far as if it were positive, particularly if the reaction is found to be still negative a week after a provocative injection of, say, 0·3 grm. of "914." In a case where the clinical appearances suggest secondary or later syphilis, a negative reaction should cause a new clinical examination to be made, but does not weigh greatly against the clinical evidence In a case which has been treated, a negative reaction does not indicate that the patient has been cured, or even that he is near to cure, because nobody knows the amount of active syphilis which may be hidden behind the veil of a negative reaction

A doubtful reaction, sometimes returned as weakly positive, is suspicious of syphilis, but for purposes of a first diagnosis is very unsafe, since many non-specific cases give such reactions. A provocative injection followed by another test in a week is indicated, and the wise clinician will wait for more definite evidence than a doubtful reaction before labelling his patient as syphilitic. In a patient who has been diagnosed previously and treated, a doubtful reaction should be taken as an indication that the treatment was not sufficient.

A positive reaction indicates that the patient is suffering from syphilis, with some reservations. Positive reactions have been reported by various authors in the following diseases, viz.: yaws, leprosy (chiefly tuberculate), trypanosomiasis, relapsing fever, malaria, scarlet fever, tropical ulcer, pellagra, beri-beri, pneumonia, late tuberculosis, diabetes mellitus, typhoid fever, sclerodermia, and malignant tumour. A positive reaction has occasionally, also, been given by the serum of persons *in articulo mortis*, and by that of quite a large percentage of corpses, while in a few cases the serums of patients under general anæsthesia and of those in eclampsia have been positive.

Of the diseases mentioned above, yaws, leprosy, trypanosomiasis, relapsing fever, and tropical ulcer are little likely to be encountered in this country, or, with the exception of yaws, to give any trouble

in diagnosis. In pellagra, beri-beri, pneumonia, late tuberculosis, diabetes, typhoid fever, and malignant tumours, the results as to positive reactions are isolated and unconfirmed by other workers, and it is more than probable that in most of them the patient was also suffering from syphilis. The only questions likely to arise in this country concern scarlet fever, malaria, and sclerodermia. *Scarlet fever* has given the reaction in about 5 per cent. of cases, and most of these were obtained by a technique which is not now employed. *Malaria* appears in some hands to have given the reaction, but only at the height of the fever. It is very probable that the cases in which a positive reaction was given were really suffering from latent syphilis. J. Thomson and C. H. Mills investigated 130 cases of malaria and obtained eight positive reactions, but in every one of these there were stigmata of syphilis. I have tested the serums of many patients who have suffered at some time from malaria, but, apart from syphilis, have not obtained a positive reaction. *Sclerodermia* has occasionally been reported to have given a positive reaction, and one such result was obtained at Rochester Row Military Hospital in a test series.

Three other conditions, which are not mentioned above, demand closer attention because they are skin diseases which may resemble syphilis and in some laboratories may give a positive reaction. They are *psoriasis*, *urticaria pigmentosa*, and *erythema iris*. I have seen cases of these diseases which gave a partial reaction, and have also seen them diagnosed as syphilis on the strength of positive reactions obtained in good laboratories.

In every case in which a positive reaction is returned and the clinical findings do not seem to agree, another specimen of blood should be taken and the test repeated before the diagnosis is made, so as to exclude the possibility of technical errors in the conduct of the test.

Although a positive reaction indicates that, with the above reservations, the patient is suffering from acute syphilis, it naturally does not indicate that every abnormality to be found in the patient is syphilitic in origin. The reaction may throw a flood of light on the case, but it would be absurd to imagine that it dispensed with clinical examination.

The above remarks will make it unnecessary to [illegible] more than briefly to the Wassermann test in the diagnosis [illegible] lesions. It will be understood th[illegible] is always [illegible] ise of suspected syphilis.

Cerebro-spinal fl[illegible] of a W[illegible] of the blood-serum is no in[illegible]on of the [illegible] system. In any case pr[illegible] *s suspiciou*[illegible]

brain or spinal cord an examination of the cerebro-spinal fluid is indicated. Similarly, before pronouncing a patient cured, not only the blood-serum but the cerebro-spinal fluid must show no evidence of syphilis.

The changes which occur in the cerebro-spinal fluid in syphilis of the central nervous system are:

1. An increase of lymphocytes to more than 5 per c.mm.; this occurs also in other diseases, e.g. tuberculous meningitis.
2. An increase of globulin and albumin, a change which is also found in other diseases.
3. The Wassermann reaction becomes positive. The fluid is usually tested in much larger amounts than the blood-serum—five to ten times as much. A positive reaction is diagnostic of syphilis.
4. Lange's gold test, in which the fluid is diluted in arithmetical progression and added in each dilution to a constant amount of a colloidal gold solution.

Lange's gold test is believed to add to the knowledge gained from the other tests. Thus it is impossible to tell from other tests whether the fluid is from a general paretic, but it is claimed for the colloidal gold test that it will distinguish between a paretic fluid and one from a case of syphilis of the supporting structures. In the case of the paretic the fluid in the lowest dilutions, 1 : 10, 1 : 20, 1 : 40, 1 : 80, causes a change of the colloidal gold solution (which is wine-red) through varying degrees of blue to complete decolorization, while the liquid in the tubes containing the remaining dilutions, to 1 : 2,560, remains unchanged. This is called the *paretic curve*. In a case of syphilis of the supporting structures of the central nervous system the dilutions of 1 : 10 and 1 : 20 cerebro-spinal fluid do not change the colloidal gold solution, and the colour changes are found in the tubes containing dilutions ranging from 1 : 40 to about 1 : 160. This is termed the *luetic curve*. In the writer's experience the fluid of general paretics does give a paretic curve, but more evidence is necessary before a paretic curve can be regarded as diagnostic of general paresis.

No changes may be found in the fluid in some cases showing symptoms of syphilis of the central nervous system. Such cases are usually syphilitic arteritis, arrested tabes, or arrested disease of the supporting structures. The general belief at present is that, if in the fourth year from infection and at least a year from suspension of treatment, the fluid is negative, it will not revert to positive. Time will show the truth or otherwise of this belief. The only thing which is certain, in the writer's belief, is that a positive fluid indicates active disease and calls for treatment. A negative fluid in the presence of active clinical signs is very strong, but not absolute evidence against active syphilis of the central nervous system.

THE PRIMARY LESION: CLINICAL CHARACTERISTICS

The primary sore is usually situated on some part of the external genitals, appearing first as a small papule. The subsequent course and clinical features depend somewhat on the consistency of the affected tissues, and whether they are kept moist or exposed to drying influences. Generally, however, it may be said that practically all primary syphilitic chancres have the following features in common:

1. *Sp pallidum* can be found in the secretion, and does not occur in any non-syphilitic lesion.
2. The edge of the sore is very slightly, if at all, raised above the surrounding surface.
3. The edge shelves gradually into the centre, and, at the junction of the edge with the central, abraded, or superficially necrosed portion, a rose-pink band, or areola, about ½ mm. or more broad, can usually be seen.
4. The tissues around the sore are commonly infiltrated and matted together with the sore into a lesion which feels stiff and rubbery, can be moved as one mass, and on pinching does not buckle so easily as an ordinary septic lesion
5. The sore usually causes much less discomfort than an ordinary sore.
6. The nearest lymph-glands usually become painlessly enlarged.
7. The sore follows an exposure to infection more than nine days previously.

Characters of the chancre in different situations.

At the mouth of the prepuce.—One or more radiating fissures may have become infected, and the depth and length of the sore depend on the size of the original fissure In any case the latter becomes converted into a furrow with a rather gaping mouth and stiffened slopes, which are usually livid red in colour. In other cases a large proportion of the circumference of the prepuce may be affected, and the orifice is converted into an indurated ring which prevents retraction The individual sore may appear on the surface with a slightly depressed margin

On the mucous surface of the prepuce the chancre is seen in its most characteristic form at the junction of the prepuce with the coronal sulcus. Here the sore occupies the borders of the sulcus for a variable distance, spreading crescent-wise into the prepuce and glans respectively, the horns of the crescent embracing the coronal sulcus, where the base of the sore is ragged and rather hæmorrhagic, with small trabeculæ bridging the gap. The erosion spreads more widely on to the prepuce than the glans, and usually appears either dull-red, or glistening white with flecks of red, according to

its age. Induration is a prominent feature, so that, when the prepuce is retracted, the whole sore flicks over like a plate turning on its edge. When a primary lesion is situated between the free edge of the prepuce and the coronal reflection there may be very little erosion or ulceration, and the lesion becomes apparent as a cartilage-like "button" let into the tissues. This also flicks over in characteristic fashion when the prepuce is retracted.

On the **surface of the glans** the flat papule spreads in an evenly circular manner to the size of about a threepenny-bit. The centre is superficially eroded, and usually occupied by a white pellicle, removal of which reveals a rose-pink, moist surface. The centre is bordered by a characteristic pink band of varying width, and sharply defined from the surrounding surface. Induration is present, but not easily appreciated owing to the tightness and shallowness of the infected tissue.

At the **meatus** the appearances are similar to those on the surface of the glans. A sore may have one edge only resting on the meatus and mainly occupy one wall of the fossa navicularis. In this situation it is often overlooked, and the slight urethral discharge accompanying it may be attributed to gonorrhœa. Apart from the characteristics of the visible edge of the sore, it is easily recognized by palpating the walls of the fossa with a finger and thumb placed at right angles to the long axis of the penis. The indurated wall of the fossa feels then like a plate which can be rocked by its edges between the palpating finger and thumb.

On the **skin of the penis or the scrotum** the sore is usually oval and covered with a blackish crust. Removal of the crust reveals a superficially ulcerated, granulating surface. The ulceration is usually deeper at the peno-scrotal angle, and the sore here is more painful than elsewhere on the penis, owing doubtless to the frequent bending and stretching to which this part is subjected. Induration is an early feature, but the examiner should not expect to find here a cartilaginous "button" such as he would find under the prepuce. The palpating finger easily appreciates a building-up and thickening of a narrow zone of tissue around the erosion, and also that the whole lesion is matted together into a plaque of rubber-like consistence. Sores on the skin of the penis at the preputial margin and on the labia tend more than any others to give rise to a characteristic œdema of the penis—*syphilitic indurative œdema*. The soft tissues distal to the sore become swollen and tougher than normal, and appear somewhat livid, while the surface of the skin shows patches of very light scaling.

Complications of penile chancres.—A chancre occupying the mouth of the prepuce, or one below the prepuce with its zone of

induration spreading to the margin, commonly causes or increases phimosis, and the pent-up secretions in the preputial sac, with their *hordes of micro-organisms, are then apt to lead to secondary infection.* Septic infection of a sore may lead to deeper ulceration than normal, and the inguinal glands may become painful and even suppurate. The most serious complication arises from special infection of a sore beneath a tight prepuce (possibly by anaerobic organisms), resulting in a swiftly spreading phagedæna. The ulcer becomes blackened, quickly perforates the prepuce, and spreads deeply into the tissues of the penis, causing very rapid and extensive *destruction of the parts. It is fortunately a very rare complication.*

Chancres of the female genitalia.—These chancres are very similar to those found in the male, but are often more difficult to find. The sore outside the labia is similar to that of the skin of the penis. On the mucous surface of the labia and the anterior commissure it is similar to that found on the glans penis; on the posterior commissure, where the tissues are looser, there is usually more induration. Sores here tend more easily to be secondarily *infected, and are thus apt to lose many of their syphilitic characteristics.* Syphilitic indurative œdema is more common in women than in men, one or both labia swelling considerably as a result of the lymphatic obstruction.

Chancre of the cervical orifice is an erosion with a well-defined margin occupied by the characteristic areola. Induration can be appreciated by palpation, especially when the sore is in an advanced stage. The lymphatic drainage being towards the pelvic glands, *inguinal adenitis does not occur.*

Diagnosis of genital chancres.—I have seen so many disastrous consequences of mistakes made by workers of the highest repute, relying on clinical examination alone, disasters in the form of aneurysm, tabes, and general paresis in patients who had been assured by eminent specialists that the original sore was not syphilitic, that I strongly recommend resort to microscopic examination in every case. The secretion is obtained, after swabbing the part with wool or gauze wrung out in saline, by scraping the margin of the sore with a spud, a vaccination lancet, or a scalpel. If antiseptics have been applied, or the sore is beginning to heal, it is advisable to push the point of the instrument *deeply into the tissues. The sore is squeezed,* and as soon as the blood has stopped oozing, the specimen is collected either on a coverslip if it is to be examined at once, or in a capillary tube if it is to be sent away. If the sore has been treated *with antiseptics* and the specimen has to be sent away, it is wise to take also a specimen from an enlarged gland. This is easily carried out. A fairly stout, hollow needle is run obliquely into the gland from above

downwards and inwards, and when it is judged that the point is well into the gland, the point is moved about by rocking the needle round its short axis A syringe containing about 5 min. of boiled water is attached to the needle, the water injected, and the gland well massaged. Suction is then applied to the needle by means of the syringe and maintained as the needle is withdrawn. The contents of the needle are expelled into a watch-glass, or on to the surface of a glass slide, and collected as above.

Clinical diagnosis.—Clinically, other genital lesions are distinguished from syphilitic chancre as follows:—

Balanitis is a superficial exfoliation with no definite border and no induration. *Herpes* is a collection of pin-head vesicles which become minute sores. It is often preceded by some irritation, and comes and goes. The border of the composite lesion made up of the margins of minute sores is polycyclic, and there is no induration. The runs of *scabies* are mound-like, often with slight linear scabs. Evidence of scabies can usually be found elsewhere. There is no surrounding induration, and no central erosion or areola. *Secondary syphilitic lesions* are usually flat, not eroded, not indurated, and unaccompanied by such pronounced local adenitis as the primary sore.

Soft chancre, or *chancroid,* has a margin which is usually more irregular than that of the syphilitic chancre. The edge is more or less undermined, and the surrounding tissues preserve their normal appearance to the very edge of the ulcer. In some cases the tissues bordering on the sore rise precipitously so that the whole lesion forms a small plateau like a truncated sea-anemone. The base of a soft chancre is usually cribriform, and more deeply ulcerated, and leaves a fibrous scar Syphilitic sores may also leave scars, but these are more plastic. If no scar is left, or a mere stain, it suggests that the original sore was syphilitic. Soft chancres under the prepuce or within the vulva are rarely single; usually there is one large ulcer accompanied by a number of smaller ones of varying size. Syphilitic chancre may be multiple, but a single sore under the prepuce or within the vulva suggests syphilis. The tissues surrounding a soft chancre are not indurated; the sore itself may become rather hard as it heals, but by this time a syphilitic sore would usually have become matted up with the surrounding tissues into a rubber-like plaque. Soft chancre is usually very painful when handled. A syphilitic chancre may be rather painful, but can usually be handled with comparatively little discomfort. If the neighbouring glands, though large, are not very painful and the skin over them is not reddened, syphilis is strongly suggested. If they are painful, or even suppurating, syphilis is not thereby excluded. If the patient is

reliable and admits only a single exposure, an incubation period of less than a week suggests soft chancre. One of more than a week suggests syphilis, but does not exclude soft chancre.

With all this, it must be remembered that a person may be doubly infected by one exposure. Soft chancre appears first, but syphilis may be incubating in the sore. Consequently no case should be dismissed at once as one of soft chancre. The sore should be watched carefully, and for this reason it is better to dress it with hypertonic saline (2-per-cent. sodium chloride with 1-per-cent. sodium citrate), so that microscopical specimens can be taken later if a suspicion of syphilis should arise; such a dressing is as good as any for most soft chancres. When syphilis appears the edges round off and the surrounding tissues begin to become tougher. I make it a rule not to dismiss a case of genital sore with a diagnosis of soft chancre until no sign of syphilis has appeared for three months and the Wassermann reaction has remained negative.

Extragenital chancres.—The proportion of extragenital to genital chancres is low. White and Brown, in an analysis of 9,000 early cases of syphilis in the British Expeditionary Force, France, found 0·91 per cent. of chancres to be extragenital in origin. The writer found 3·5 per cent. in 1,500 early cases in civilians; Fournier, 6·3 per cent., and Hahn for Germany, France, and Denmark, 4·5—5·5 per cent. The incidence of extragenital chancres varies with the conditions under which the population lives. Thus in certain provinces in Russia where the members of families live in close contiguity it has been estimated at 74 to 92 per cent. (Finger).

Extragenital chancres are frequently overlooked simply because the surgeon forgets that there is such a disease as syphilis. It cannot be too strongly insisted that, on the slightest suspicion that a sore on some part of the body is a chancre, a specimen of the secretion should be examined without delay. A valuable clue to an extragenital chancre is often afforded by an indolently enlarged group of glands, the corresponding glands on the opposite side of the body being normal, or not greatly increased, in size. An extragenital chancre may occur anywhere on the skin or visible mucous membrane, even well inside the nose; over 70 per cent. occur in the head area, and over 50 per cent. on the lips.

Chancre of the anus may affect the margin as an indurated, dull-red fissure, or a definite sore, partly within and partly outside the anal orifice. It is distinguished by its well-defined, indurated margin. The glands in the outer third of the inguinal region are indolently enlarged. In the rectum a chancre is often overlooked unless an abnormal discharge, or the appearance of other signs of syphilis, provokes an examination. The finger feels a fairly well-

defined disc with a slightly depressed centre. Through the speculum the sore appears as a single lesion standing out from an intact mucous membrane.

Chancre of the skin in most parts of the body is like chancre on the skin of the penis or scrotum, a round or oval, slightly raised, indolent sore covered with a dark crust, removal of which reveals a dull-red granulating surface. Enlargement of the nearest lymph-glands is a valuable clue. On the **finger**, other than the ends, it may appear as a superficial erosion, or a flat, scaly papule, with very slight induration. On the **ball of the thumb**, or the **ends of the fingers**, the appearances suggest whitlow so strongly that syphilitic chancre in this situation is often overlooked. An infected crack at the margin of the nail develops into an indolent ulcer with dull-red granulations, which may spread around the nail margin. In other cases the terminal phalanx becomes deep-red, brawny, and bulbous. The pain may be very severe The epitrochlear glands are usually enlarged, but may be skipped and the enlargement affect only the axillary glands.

Diagnosis.—An indolent sore on a finger or thumb, or in fact on the skin anywhere, should arouse a suspicion of syphilis and cause a microscopical examination of the secretion to be made without delay. If the sore has been dressed with antiseptics, an enlarged epitrochlear or axillary gland should be punctured. It is important not to exclude syphilis on the ground of pain, since, in the case of chancre of a terminal phalanx, this may be excruciating. It should also be remember[illegible]

Chancre of [illegible]

portion of the lip [illegible]

shows the erosion or ulceration on the moist side of the lip. The mass is more or less raised, with a slightly indented centre, and the surrounding tissues are thickened and toughened. It is diagnosed from *impetigo* mainly by the depth of infiltration and toughening of the tissues, and by the painless enlargement of the neighbouring glands *Epithelioma* is much slower in growth; its surface is far more irregular, and its edge is as much harder as an unripe pear is harder than soft rubber, while glandular enlargement is slower in development and not so pronounced.

Lingual chancre is easily recognized as a well-defined sore raised above the surrounding mucous membrane. The centre is eroded and slightly cupped, and the whole lesion indurated. It is usually situated somewhere near the tip. The submental glands quickly become enlarged. It is fairly easily diagnosed from *epithelioma* by the quickness of its growth, absence of pain, situation, and the rapid enlargement of glands. The edges are not so hard as in epithelioma,

nor is the surface so ragged *Tuberculous ulcer* is softer and more irregular in outline, and its edges are undermined.

A tonsillar chancre is often diagnosed as simple tonsillitis until secondary symptoms appear. The tonsil is much enlarged and indurated, and the marked enlargement *of submaxillary glands on* one side should arouse suspicion.

Chancre of the eyelid may appear as a pink papule at the inner canthus. The entire lid may become infiltrated and considerably swollen. The preauricular glands enlarge, but may not be very palpable.

Chancre of the conjunctiva is rare. It begins as a papule and grows into a round or oval, elevated sore, which is superficially eroded. Suspicion may be aroused by the fact that the patient is otherwise in good health, and by the indolence of the sore.

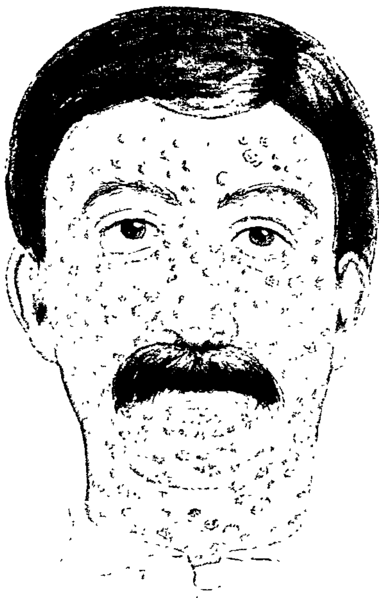
Chancre of the mouth of the Eustachian tube has been recorded in a fairly considerable number of cases, infection having been conveyed by a Eustachian catheter.

Adenitis, first affecting the glands adjoining the primary sore, and later all the palpable glands, is very characteristic of syphilis. The enlargement due to the primary sore is usually much greater than that seen in general adenitis, and a group of unilaterally enlarged glands is often a useful clue to the situation of an extragenital chancre. *As a rule, the glands remain smooth and discrete, though enlarged,* oval, and indurated. In general adenitis the epitrochlear, axillary, and cervical glands are those usually palpated.

RASHES ARE OTHER MANIFESTATIONS OF THE SO-CALLED SECONDARY STAGE

Just before the outbreak of the first skin rash the soft palate often becomes erythematous. Characteristically, the erythema is rose-red, and contrasts strongly with the pallor of the hard palate.

The first rash to appear, the **roseolar or macular syphilide,** is made up of pink or darker-red spots varying in size from a threepenny-bit to a florin, which at first show *dimly through the* epidermal covering. The spots usually appear first on the flanks between the level of the scapular angles and the iliac crest, and spread over the abdomen and back, and then over the limbs, the back of the neck, and occasionally the face. Similar spots may be seen on the glans penis, and occasionally a few may appear on the soft palate. In general appearance the rash simulates fairly closely that of measles. In typical cases the skin looks slightly urticarial (syphilitic urticaria). The rash, like other skin manifestations of syphilis, *is accompanied* by little or no itching. The spots are often so dim that the patient does not notice them, and they may not be



Lenticular syphilide. (*Wilfrid Fox's case.*)

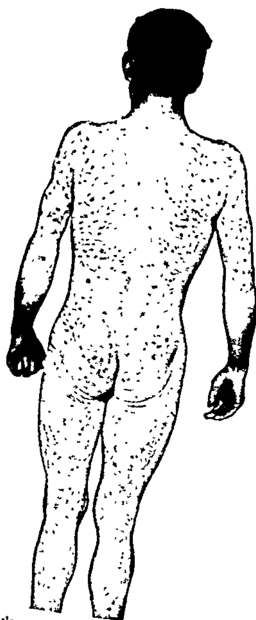
PLATE 69.

to be divided into primary, secondary, and tertiary stages mainly because the *great majority of cases show* (1) *a primary sore* (2) a roseola followed by an ordinary type of papular eruption, which is succeeded by a long period of latency, and then (3) one or more large gummatous lesions which differ strikingly in appearance from the ordinary papular eruption. If the lesions of all cases are considered, such a division is impossible, since there is little to distinguish some late papular from some early gummatous syphilides.

In point of time, papular syphilides usually range over the period from three months to two years from the appearance of the sore, but in odd cases the first papular eruption may be seen earlier, and in other uncommon cases manifestations of syphilis which can be classed as of the papular type may be found a number of years after infection. The earliest type, and that most commonly seen, is the dome-shaped, or lenticular, papular eruption (Plate 70), consisting of rose-red spots well embedded in the skin. The usual size is about that of *a split pea, but mixed up with these papules may be some which* are as small as a pin's head, and there may also be a fair number which are considerably larger, while in such places as the fronts of the forearms and the abdomen they may appear as large, brownish-red plaques the size of a shilling or bigger. *The distribution on the* trunk and limbs follows closely that of the macular syphilide, but may be much wider, extending to the face, scalp, genitalia, between the buttocks, palms, and soles. Papules can often be seen springing from the centres of macules The spots vary in number, but usually are less numerous than those of the macular syphilide. In some cases only a few papules can be found over the whole body, but in others a half-crown placed anywhere on the trunk would easily cover two papules. The clinical appearances of the papular eruption vary with its situation and with the subject. On the trunk and dry parts of the limbs the typical papule is a dry, slightly elevated, cherry-red spot, which becomes deeper-red and browner with age. When picked up between finger and thumb it feels rubbery and well embedded in the skin. When it is squeezed the surface blanches and the epidermis glistens, as if the superficial layers were *slightly separated from* those below. At the same time the surface usually cracks slightly, and light brushing with a finger-tip causes a scale to become slightly detached. In other cases the scale is more obvious, the papule becoming silvery white in the centre. The scales can be *brushed away fairly* easily, *or* are *removed by friction* with the clothing, leaving a collarette or loose fringe of epithelium around the margin (*papulo-squamous syphilide*). *A further degree* is the *squamous syphilide*, where the majority of the papules are completely covered by silvery *scales (Plate 71). Scaling is usually a* prominent



Maculo-papular syphilide.



Papulo-maculo-squamous syphilide.

PLATE 71.

Diagnosis of papular, pustular, and ecthymatous syphilides.—The chief distinguishing characteristics of syphilides of this stage are:

(1) Their pleomorphism, several varieties of lesions with characters suggestive of syphilis being present on the same subject.

(2) The absence of any marked signs of irritation.

(3) The deep foundation of the ordinary papule, its smoothness, its blanched, glistening appearance when it is squeezed, and the cracking of its superficial epithelium.

(4) The disc- or ring-like shape of the lesion on the scrotum, its moisture, and the glistening appearance of its rim when the skin is put on the stretch.

(5) The broad, wart-like appearance of the condyloma, or the rose-red, moist plaque often found between the buttocks when condylomas have not formed.

(6) The fringe or collarette of loosened epithelium around the moist papules between the toes, under the *mammæ*, and in other moist situations, and around the squamous syphilide found on the palms and soles and elsewhere. The collarette surrounds a glistening, rose-pink area.

(7) The rim of syphilitic, papule-like tissue around the papulo-pustule.

(8) The characteristic grouping of the lesions of the follicular syphilides.

(9) The circular or oval, rather than linear, shape of the crusted syphilide.

(10) The presence of *Sp. pallidum* in the secretion. The last is the most practicable and reliable method of clinching the diagnosis of a syphilide of this age of infection, though it is perhaps less applicable to rupia, corymbose and small follicular syphilides, which, however, appear only in a minority of cases. It is necessary only to scrape off the superficial epithelium and squeeze the lesion to express serum from it.

Psoriasis differs from the squamous syphilide in being drier and rather more superficial. The scales are usually more closely set and silvery, especially on light scraping, which also produces oozing of blood at several pin-points. The eruption is true to type all over, and affects more particularly the extensor surfaces.

Lichen ruber planus differs from the papular syphilide in the polygonal shape of the spots, their confluence, violaceous tint and waxy appearance, and in their irritability. The anterior surfaces of the wrists, forearms, and legs, and nape of the neck are favourite situations

In *scabies* any raised lesions are mainly pale, not red and glistening,

and may show *obvious signs of scratching in bloody points and lines. Any scabbing is very superficial.*

Blind acne spots are usually more inflammatory and painful when squeezed, and a drop of pus can generally be expressed from them when they are pricked with a needle.

Molluscum contagiosum spots are white and umbilicated, and caseous matter can be squeezed from them.

Lichen scrofulosorum is distinguished from the miliary syphilide *by occurring in younger subjects, of a tuberculous type, and by the absence of other signs suggestive of syphilis.*

Ringworm differs from an annular syphilide in being more in*flammatory and more superficial,* as well as in its slightly vesicular *border, its irritability,* and the presence of the fungus.

Tinea cruris (dhobie's itch) on the upper and inner side of the thigh *is more superficial than a* secondary plaque; it is also more irritable, *and the fungus can be found in the scrapings*

Variola is distinguished from the generalized pustular syphilide *by the preceding fever* and constitutional disturbance, the similarity of the lesions all over the body, the acuteness of development and progress, the tendency to favour the face, backs of the hands and wrists, and the absence of *Sp. pallidum.*

Bromide and iodide eruptions are associated with the taking of *these remedies* and are more acute and inflammatory. In cases of *suspicion* as to the taking of patent medicines, a little hydrochloric *acid should be added* to the urine, which is then shaken up with chloroform. Bromide tinges the chloroform yellow, and iodide violet.

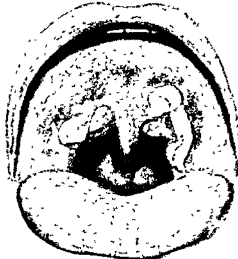


Fig. 1.—Mucous plaques on the isthmus of the fauces.



Fig. 2.—Mucous plaques on the under surface of the tongue

(From P. H. Gerber's "Die Syphilis der Nase, des Halses und des Ohres.")

PLATE 73.

of confluent papules which differ in appearance from similar lesions on the skin because of the moisture and friction to which the former are exposed. The typical mucous patch is seen on the pillars of the fauces, or on the mucous surfaces of the lips. It is a greyish-white, flat lesion, which is round or oval within the lips and covers the faucial pillar like a snail track. The greyish-white centre is bordered by a rose-pink band which is flush with the surface and sharply defined from the surrounding mucous membrane. In some cases the sodden, greyish centre of a mucous patch within the lip is removed by friction, and the whole lesion is then rose-red.

In situations where the lesion is exposed to squeezing or stretching, as on the tonsil, the sides of the tongue, and the angles of the mouth, there is usually some fissuring and ulceration. The tonsils may be fairly deeply ulcerated. On the sides of the tongue appear grey, circular erosions, or fairly deep fissures following the furrows, often covered by a white adherent pellicle and sometimes surrounded by a patch of leucoplakia. On the dorsum of the tongue smooth red patches or rings, which look as if the papillæ had been rubbed down with pumice stone, may be seen during the stage of the papular eruption. Occasionally the lesions on the tongue are more vegetative, and condylomata are found on the posterior section of the dorsum or on the under-surface. At the angles of the mouth, mucous patches practically always become fissures, and a small scab can usually be seen outside where the corner of the mouth is exposed to the air.

Diagnosis of lesions of the mouth and tongue.—Mucous patches on the fauces and tonsils may be mistaken for very mild diphtheria, for Vincent's angina, or for thrush, but any doubt can usually be settled by the microscope. In taking specimens from mouth lesions it is well to avoid, as far as possible, admixture with saliva, which may contain *Sp. dentium* (see p. 765) After swabbing with dry wool, a nasal ring curette is a very useful instrument for scraping the lesion and gathering the specimen.

In *diphtheria* the covering pellicle can be loosened more easily at its edges, and the denuded surface bleeds more readily. The fauces are usually more reddened, and the submaxillary glands enlarged.

Vincent's angina may resemble a mucous patch rather closely, as there may be little or no general disturbance. The edge of the lesion looks more angry, not pink, and when the pellicle is rubbed with a swab the surface below bleeds easily.

Thrush may cause a white membrane on the soft palate, but when this is brushed away the surface below looks fairly normal.

Secondary lesions of the tongue may be mistaken for herpes, tuberculous ulceration, exfoliative glossitis, primary syphilitic lesions, or syphilitic leucoplakia. *Herpes* appears in crops of very small

superficial vesicles which are sufficiently characteristic, when examined closely, to be distinguished from secondary lesions of the side of the tongue. The spots tend to recur, and are often preceded by some neuralgic pain. The *tuberculous ulcer* is more painful, ragged, and undermined, and is usually associated with advanced tuberculosis. *Exfoliative glossitis*, or wandering rash, has a fine white, gyrate border, which is constantly shifting. *Primary syphilitic lesions* of the tongue are single, stand out boldly, and are accompanied by well-marked local adenitis. *Tertiary glossitis* and *leucoplakia* are much tougher lesions than those found in the earlier stages of the disease.

Laryngitis is fairly commonly seen in patients with a papular eruption. Occasionally it occurs without other manifestations, and is then usually overlooked A chronic laryngitis without great discomfort or constitutional disturbance should arouse a suspicion of syphilis.

The hair.—The papular syphilide is often accompanied by considerable loss of hair, which may result in the patient becoming temporarily bald. More commonly the loss is patchy, so that the scalp at the back and sides looks like a moth-eaten fur.

The **nails and nail-beds** are rarely affected, and as a rule only after about six months. When the nail itself is diseased (*onychia*) it may become dry, brittle, furrowed, and pitted in parts, tending to split easily. Or an opaque spot forms, followed by a pit in the nail. The nail may be longitudinally striated *Perionychia* may be manifested by thickening and scaliness of the tissues around the nail, or there may be diffuse, dusky reddening and swelling of the finger-ends, and the tissues bordering the nails are fissured, oozing serum and showing granulations in parts.

Bones.—In the early stage, almost before the rash appears, periostitis may cause considerable aching in the bones, especially at night. Occasionally, at a rather later date in the first year, a painful node forms as a small, elastic swelling on the surface of the bone. Unless treated, it may become a bony nodule. The tibia, ulna, clavicle, sternum, cranial bones, and ribs are those usually affected.

Synovial membranes of joints, tendon sheaths, and bursæ are rarely affected during the early stages. There may be a good deal of effusion and pain, with fever; more commonly the effusion is quiet, with a moderate amount of tenderness but a freely movable joint. The elbows and knees are the joints in which syphilitic synovitis occurs most frequently.

The eyes.—Occasionally a mucous patch occurs on the conjunctival surface. **Iritis** and **irido-cyclitis** are not uncommon during the first year, but may also occur considerably later. The

eye becomes reddened, with a good deal of circumcorneal congestion and photophobia. The iris loses its lustre, and there may be a plastic effusion into the anterior chamber. There is a great tendency to posterior synechiæ, and the many cases seen with a permanently contracted pupil testify to the frequent failure to recognize syphilitic iritis before the iris has become permanently adherent to the lens.

Choroiditis and retinitis also occur in secondary syphilis and often remain unrecognized until the patient is fortunate enough to meet someone who remembers the existence of such a disease as syphilis.

Interstitial keratitis is a very rare manifestation of acquired syphilis, it will be described under Congenital Syphilis (p. 834).

Neuro-keratitis, with resulting opacity and ulceration of the cornea, is rare. It results from syphilitic involvement of the ophthalmic branch of the 5th nerve, and is associated with anæsthesia of the conjunctiva and temple.

The **ears** may suffer in the early stages of syphilis from blockage of the Eustachian tube consequent on the naso-pharyngeal catarrh. A mild otitis media may be the result of a syphilitic eruption of the mucous membrane. It is possible also that syphilitic naso-pharyngeal catarrh and ulceration may predispose to secondary suppurative otitis media.

Of much more importance is the deafness which may develop at almost any time during the course of syphilis, though it is very uncommon before about the third month. In fairly recent cases the onset may be sudden, with preliminary hyperacousis, followed by rapid loss of hearing, distressing tinnitus, and vertigo. In older cases the development is more gradual, and may be unaccompanied by tinnitus or vertigo.

The acute form, occurring from three to twelve months after infection, became much more common just after the introduction of salvarsan treatment, when many cases were being injected with only one or two doses of the new remedy in the belief that this was sufficient to eradicate the disease. It was very often associated with paralysis of the facial nerve and with pathological signs in the cerebro-spinal fluid indicating syphilitic meningitis. The fact that, at this time, syphilitic affections of other cranial nerves, such as the 3rd and 5th, became more common, makes it clear that the cause of acute syphilitic deafness developing comparatively early in the history of the infection lies generally in infiltration of the nerve-trunk accompanying basal meningitis. At the same time, it is necessary to mention Moos's case, quoted by West, of early syphilitic deafness in which the auditory nerve-trunk was intact and the condition found was a syphilitic labyrinthitis.

Early acute syphilitic deafness has again become very uncommon, as it is now usual to administer much more treatment than was thought to be necessary just after the introduction of salvarsan; but the experience of those earlier years shows clearly the danger to the central nervous system, including important sense-organs, of an insufficient arsenobenzol treatment

It may be convenient here to deal with deafness in the later stages. Usually in such cases the affection is a syphilitic meningitis involving the 8th nerve. The onset and course are much more insidious than in the earlier stages, and the syphilitic origin is often overlooked. Much less commonly, gummata of the mastoid and other portions of the temporal bone may lead to involvement of the middle or internal ear and to consequent deafness

The deafness of adolescents suffering from congenital syphilis is considered in the article on Congenital Syphilis (p. 835). In tabes and general paresis the auditory nerve may very rarely be involved in a manner analogous to primary optic atrophy. Hyperacousis may be early, and accompanied by tinnitus and vertigo, which are followed by deafness.

The **testicle** is rarely affected in the early stages of syphilis. Not very uncommonly one or two nodules appear in the globus major of the epididymis. The affection is distinguished from gonococcal and tuberculous epididymitis by absence of history of these diseases and by its situation in the globus major (*See also* Vol. II., p. 982.)

The veins.—Very early, or during the first year, syphilitic phlebitis may cause round or spindle-shaped nodules in the veins. Such a nodule becomes adherent to the skin, which reddens over an area about the size of a shilling, and may break down to an ulcer with overhanging edges and discharging sanious pus. Syphilitic phlebitis is commoner in women, and occurs most often on the legs.

Early syphilitic affections of the **viscera** and **central nervous system** concern more particularly the physician, and require only brief mention here. **Nephritis** is uncommon in the secondary stage; it is important in connexion with treatment. It is said to be accompanied very rarely by œdema, and may end in death from uræmia, though no such case came to my notice among the 100,000 or so soldiers treated for syphilis during the War. **Acute yellow atrophy of the liver** is a very rare sequel of syphilis. ***Mild gastro-intestinal disturbances*** are becoming more and more recognized as accompaniments of early syphilis. ***Syphilitic meningitis,*** meningo-myelitis, myelitis, and meningo-encephalitis are important possibilities. The central nervous system is invaded early in a large proportion of cases. In a small proportion of these, clinical manifestations may appear as early as the third month, or any time later,

in the form of isolated nerve disturbances, or as system paralyses. They are usually the penalty of insufficient treatment, especially of reliance on a comparatively small amount of arsenobenzol. Their relation to eye and ear disturbances has been discussed (*see* p. 789).

The **anæmia and general constitutional disturbance** which accompany early syphilis have been sufficiently described (p. 763).

TERTIARY LESIONS

After the secondary rash has faded, the syphilitic may manifest no outward sign of his disease for many years, or even throughout a long life Many patients appear with a late syphilitic lesion who have no recollection of a sore, rash, or other sign of syphilis, but admit gonorrhœa twenty or thirty years previously. The probability was that the " gonorrhœa " was, or was associated with, primary syphilis in the form of chancre within the fossa navicularis, and that the roseola passed unnoticed. The tertiary lesion seems always to begin on the site of some injury, though a slight one, or in a part exposed to strain or stress. The individual lesion is circular, and is generally larger, harder, and more deeply embedded than a secondary lesion; it also tends more easily to break down in the centre, discharging its gummy contents and leaving a punched-out ulcer with precipitous edges. Resolution of parts which do not break down is rarely complete, and the result is considerable fibrosis or osteosis, according to the tissue affected.

The **skin** is the tissue most commonly affected in tertiary syphilis, and the result is the **nodular cutaneous syphilide.** The individual lesion is a deep-red nodule about the width of a shirt-front button The surface may be covered with a scale or a light scab, or in rare instances the centre may break down into an ulcer. After remaining unchanged for months the nodule may gradually retrogress without treatment, leaving a slightly depressed centre with a pigmented border More often the single nodule is followed by a ring of similar nodules set concentrically with it, about half an inch out, and each of these may in turn become the centre of a circle, or segment of a circle, of satellite nodules. As fresh nodules develop, their parents, so to speak, retrogress, and the result is a lesion made up of numerous circles or segments of circles which cut into one another, or are regularly concentric. The border is gyrate or serpiginous, and covered with scales or a scab. Much more rarely the border is ulcerated along its whole length, or in short sections, so that a clean-cut trench is formed. In the centres of the numerous circles enclosed by, or in the wake of, the active border can be seen the remains of nodules in the form of pigmented spots around which

is a tissue-paper-like scar that is soft and flexible. This may be quite white except for the deposits of pigment, or may remain reddened for a considerable time. *The scars are separated from one another by* bands of normal skin. The process may stop at any stage without treatment, and continue its advance after remaining quiescent for a variable period, and so on indefinitely for many years, until a large portion of a limb or of the trunk has been affected. (Plate 74.) Once the lesion has passed a spot, *it does not recur there.* Sometimes ulceration is a pronounced feature, and the lesion advances more quickly than the healing process, so that a large area is left studded by numerous punched-out, shallow ulcers. (Plate 74.) When the ulcerative lesion affects the lips it may become phagedænic and result in a very rapid destruction of the parts. *As a rule, the* ordinary lesion is easily arrested by treatment.

Diagnosis of tertiary skin lesions.—The main difficulties arise when the lesion appears on the face. *Lupus vulgaris* occurs usually in younger subjects who are delicate and possibly show other stigmata of tuberculosis. Lupus grows much more slowly, and its border is irregular. The edge of the ulcer is irregular, not punched-out, leaves a more fibrous cicatrix scored with telangiectases, and active nodules are often *left in the scar. Also the lupus nodule is* softer and shines like apple jelly through a glass slide pressed on it, while the syphilitic nodule is hard and appears through a glass slide as a brownish stain. *Scrofuloderma* is distinguished by the irregular, overhanging edges of its ulcers, the connexion and association of these with tuberculous processes, *and the fibrous scar which is left* on healing. Tubercle bacilli may be found in the exudate. *Lupus erythematosus* usually sits astride the nose and cheeks as a butterfly might, and there are outlying patches on the tips of the ears and hands. The edge, though well defined, is not infiltrated. The scarring is much slighter. *Ringworm* is much more superficial, and leaves no scar in its wake. *Seborrhœic dermatitis* often has a gyrate border, but the lesion is quite superficial, is not infiltrated, and leaves no scar. *Malignant disease is very slow in growth and has a rolled,* very hard margin, not clean-cut like the nodular cutaneous ulcer. *Malignant pustule* (anthrax) is a far more acute process; it has a central black eschar, with surrounding vesicles, and itches intensely. Anthrax bacilli can easily be demonstrated in the secretion. *Actinomycosis* is very unlikely to be mistaken for a nodular syphilide; it is distinguished by its fistulous orifices, the puckering of the involved area, and the golden-yellow, granular discharge containing the ray fungus.

Subcutaneous gummata appear as rubber-like nodules below the skin, to which they may become adherent. The gumma may



Gummatous syphilide with rupia.

PLATE 74

ak down, leaving a punched-out ulcer with rather overhanging ;es. The ulcer might be confused with that found in *Bazin's ease*, a tuberculous granuloma which most often affects the calves girls and young women. Apart from the youth of the patient, the sence of other signs of tuberculosis, and the absence of signs of hilis, the ulcer of Bazin's disease has a more fistulous and irregular ning.

Muscles may be occupied by gummata, or be infiltrated through-. In the latter case the eventual formation of fibrous tissue may erfere considerably with the function of the affected muscle.

The bones.—Tertiary lesions of the bones are very important, ce in some situations they may lead to great mutilation and ormity. **Localized gummatous periostitis and osteitis** are ally associated. They appear in almost all cases at the site of some ury. Any bone may be affected, but the clavicle and sternum, s, tibia, and cranial bones suffer most commonly. A smooth,

mooth, ivory-like boss, or may break down in the centre; in the ter case the centre becomes soft and diffluent, while the margin raised into a ridge of ivory-like bone. Sooner or later the skin r the centre may give way, leaving a funnel-like ulcer at the tom of which is bare bone. As there is usually some extension depth, the bone may be necrosed. In the case of the skull a disc bone may be shed, leaving the membranes bare, so that pulsation y be seen in the floor of the ulcer. General meningitis is prevented the previous formation of adhesions. Sometimes, especially on cranium, two or more ulcers may coalesce into a clover-leaf pe; or a number of ulcers may surround an area of bone which roses. Very rarely the process begins on the inner table, and the ns are those of cerebral gumma, which is described later (p. 799).

Diffuse periostitis and osteitis are not very common in uired syphilis, if the small bones of the face and nose are excepted. e affected bone becomes thickened, tender, and painful, especially night. The diagnosis is usually made on the chronicity of the cess, the patient's history, and the Wassermann reaction The *tebræ* are rarely affected. A retropharyngeal abscess may form, the spinal canal may be invaded, and very uncommonly nerve nptoms may result. Kyphosis may follow destruction of one or re vertebral bodies.

The **facial and nasal bones** are comparatively seldom olved in tertiary syphilis. Fortunately so, because the result- destruction of bone may lead to considerable mutilation and

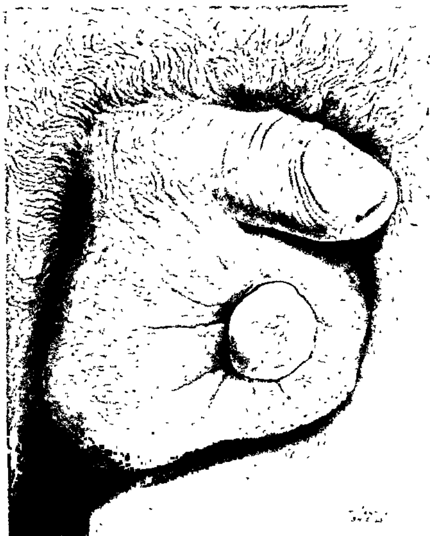
deformity. The lower and anterior part of the septum and the vomer are most commonly involved, then perhaps the hard palate. The patient develops ozæna and is constantly blowing black or greenish scabs and possibly pieces of bone from his nose. The end of the nose may be reddened and bulbous, and there may be some swelling of the eyelids and face, as well as neuralgic pains in the nose or forehead. Examination of the nares shows a swollen mucous membrane which does not collapse on the application of adrenalin or cocaine. Many ulcers may be seen. The result varies with the part affected; very uncommonly the roof is attacked, and the patient develops meningitis; more often the bridge of the nose gives way, and a saddle-nose results, or the tip falls in. In other cases a swelling forms in the roof of the mouth, and eventually the hard palate is perforated. In some cases the ulceration breaks out on the face, possibly over the nasal duct, which becomes blocked.

Diagnosis of tertiary nasal syphilis.—Chronic nasal discharge with an offensive odour should always stimulate a search for syphilis. *Lupus vulgaris* is slower, more superficial, and may be associated with signs of tuberculosis elsewhere. *Atrophic rhinitis* is not ulcerative, and the covering of the inferior turbinate bone is shrunken. *Malignant disease* is more painful; the ulcerated surface bleeds easily and is more proliferative; and adjacent glands are enlarged.

Gumma of the orbit may be easy or difficult to diagnose, according to the position of the tumour. If it is far enough forward, it may be felt as a rounded tumour; otherwise there are only the signs of intra-orbital tumour for guidance. There is dull pain in the orbit, which is worse at night, and some tenderness on pressure over the orbit or the temporal bone. The lids and conjunctiva are swollen, and there is limitation of the movements of the eye towards the affected side. This produces diplopia, which may also result from involvement of the fibres of the third nerve in the gumma. When the tumour is in the posterior part of the orbit there is some exophthalmos, and the nerves passing through the sphenoidal fissure and optic foramen are involved, with resulting papillitis and oculomotor paralysis.

The **diagnosis** rests mainly on the signs of intra-orbital tumour, with evidence of syphilis elsewhere, a positive Wassermann reaction, and the history. The safest plan is to treat on suspicion of syphilis.

Syphilitic dactylitis is a gummatous osteitis affecting one or more phalanges, especially the proximal. The phalanx gradually swells without causing any great pain and without at first affecting the tendon sheath or skin. The outcome varies. In some cases a discharging sinus forms; in others the bone becomes permanently thickened; or it may be absorbed, resulting in permanent shortening.



Gumma testis.

PLATE 75

Diagnosis of syphilitic dactylitis.—The diagnosis from *tuberculous disease* may be difficult, and in certain cases the two processes may be combined in one phalanx. The presence of tuberculosis in other parts of the body, with the absence of syphilis, and vice versa, will assist, while the skiagram will show that in syphilis the process is confined in the earlier stages to the shaft. *Enchondromata* are harder than gummata, and do not tend to soften and break down.

Synovial membranes.—A synovial membrane which is exposed to injury, as the prepatellar bursa in charwomen, a knee-joint, or an overworked tendon sheath, may become diffusely thickened, and gummatous nodules may form in it. The rubber-like thickening and the nodules can be made out fairly easily by palpation. In tendon sheaths and bursæ a gummatous mass may spread to the skin and, breaking through it, form an ulcer which may last for years. In a joint the process may attack the articular ends, which enlarge, and the joint becomes globular without particular thickening of the membrane. The disease may spread to the skin and burst externally; or ankylosis or a flail-joint may result.

The **diagnosis of gummatous synovitis** is made from the quietness of the process, the obvious thickening of the membrane, and the history.

The **testicle** is found to be involved moderately often in late syphilis Interstitial gummatous orchitis causes the testicle to become evenly enlarged, smooth, elastic, and very heavy. In addition, gummatous nodules may form, causing smooth, elastic bosses to project from the testicle. The epididymis is obscured by the enlarged testicle, and cannot be defined. A point of diagnostic importance is that testicular feeling is lost, so that the testicle may be squeezed with impunity. The condition may be associated with a hydrocele. The enlargement progresses steadily for many months, the testicle sometimes becoming many times its normal size; it may then slowly retrogress until the testicle becomes smaller than normal. Rarely, a gummatous nodule breaks down and bursts through the skin, leaving a crater-like ulcer with bluish-red, overhanging edges. (Plate 75) Occasionally a form of hernia testis occurs from the projection of granulations from the base of the ulcer. Syphilis occasionally affects the epididymis.

The **diagnosis of gumma testis** depends on the firm smoothness of the testicle, its weight and painlessness, and the absence of testicular feeling. *Tuberculous disease* affects the epididymis and cord and tends to form fistulæ. The Wassermann reaction may be negative, and there may be no history suggestive of syphilis. *Malignant disease* is usually more rapid in growth than gumma; the testicle is

tender, and testicular sensation is not lost. Any nodules are very hard. There may be no sign of syphilis elsewhere in the body.

The penis.—A gumma, often situated at the site of the original sore, is not uncommon, and may be mistaken for a primary chancre. The ulcer is typically gummatous, and adjoining glands are not enlarged. It is rare to find *Sp. pallidum* in the secretion, but recently a fair number were discovered in a case of chancriform gumma at the writer's clinic.

Mucous membranes.—The **lip** may be diffusely infiltrated or occupied by one or more gummatous nodules which may burst to form typical gummatous ulcers The gumma is distinguished from epithelioma by its clean-cut, softer edge, contrasting with the rolled, everted, very hard edge of malignant disease. A primary chancre is surrounded by more induration, the submental glands are enlarged early, and numerous spironemes can be seen in the secretion of the sore.

Inside the cheek a fairly common late sign of syphilis is a band of leucoplakia stretching from the angle of the mouth horizontally backwards for a variable distance. The affected mucous membrane is tougher, and its superficial layers are bluish-white, with light furrows cutting it up in herring-bone fashion In many cases only one side is affected, for about an inch.

The **tongue** suffers in tertiary syphilis probably more than any other part. (*See also* Vol. II)

Superficial glossitis consists in a diffuse infiltration of the submucous tissues affecting the whole or only a part of the organ. The portion affected becomes enlarged, and may be very tender, so that the patient cannot eat hot or spiced food. The papillæ disappear, leaving a red, smooth, and polished surface which may be lightly or more thickly coated with a bluish-white pellicle (*leucoplakia*). The affected area becomes lobulated, being cut up into islands by fissures of varying depth, the floors of which may be eroded. With or without the diffuse glossitis, numerous nodules may appear in the mucous membrane and ulcerate, a condition analogous to the nodular cutaneous syphilide. One or more localized gummata may be associated with diffuse glossitis, or may occur alone. They are felt as ill-defined nodules in the substance of the tongue; they may break through the mucous membrane, causing typical crateriform ulcers.

Diagnosis of syphilis of the tongue.—*Leucoplakia* is considerably denser than a mucous patch, and is bluish- rather than greyish-white. *Tuberculous ulcers* are flatter, with ragged edges, and much more painful. They usually occur in advanced tuberculosis. *Simple tumours* are well defined, elastic, and often lobulated. *Lingual cancer* has an edge which is much harder, the ulcer is much more irregular, and the edges are rolled. Cancer is often engrafted on a syphilitic

process, so that history and a positive Wassermann reaction should count as nothing in the diagnosis. Every tongue with an ulcer on it, particularly in a patient over 30, should be examined most carefully, and if there is any doubt a piece of the ulcer should be cut out for microscopical examination. The cut should extend down to the muscle.

The **palate** may be the seat of a gumma which has worked through from the nose When the gumma breaks, a perforation of the hard or soft palate is left, according to the situation. A single gumma may commence on the mouth side of the hard or soft palate. Usually the result is not severe, as the lesion attracts attention and is treated early. Perhaps more commonly than all, a nodular condition, analogous to a nodular cutaneous syphilide, affects the fauces, soft palate, and sometimes the posterior pharyngeal wall. The parts involved may be ulcerated at several points. Healing results in much deformity, with dense white scars, and sometimes the soft palate is united to the posterior pharyngeal wall.

Gumma of the **tonsil** causes a rather painful, elastic swelling, followed by a crateriform ulcer.

The **posterior pharyngeal wall** may be occupied by a single gumma which may break down to form a typical ulcer

Diagnosis.—Tertiary lesions of the fauces and palate and posterior pharyngeal wall are easily diagnosed by the history and by the quietness of the process, which is out of proportion to the extent of the lesion. It is in cases where the disease starts in the nose or nasopharynx that progressive destruction of tissue is apt to be overlooked. A valuable sign is a soft swelling of the hard palate, or a stiffened, bulging soft palate with regurgitation of food through the nose. Prompt treatment then may save the patient from a perforation A gummatous tonsil differs from an *epithelioma* in its clean-cut edges. Suspicion of epithelioma would be aroused by absence of a history of syphilis, and by eversion and hardness of the edges of the ulcer. A *primary chancre* has no previous history of syphilis, and the submaxillary glands are enlarged on the affected side.

Tertiary affections of the ear and **syphilitic deafness** have already been considered (pp 789-90).

The **larynx** may be involved in a tertiary infiltration, resulting in considerable thickening, followed by ulceration and deformity. Sometimes the ulceration spreads through to the skin. The **trachea, bronchi,** and **lungs** are rarely affected in tertiary syphilis, and then concern the physician.

The late syphilitic affections of the **heart,** gumma and myocarditis, are not of surgical interest. **Degeneration of the**

coats of the large arteries, resulting in aneurysm, is almost always a result of syphilis.

Tertiary lesions of the **stomach** and **intestines** are of interest, as their signs may simulate closely those of new growth. Recently so many cases of syphilis of the stomach simulating carcinoma have been found, that more than one worker has stated that in cases with signs of cancer and a positive Wassermann reaction he would first try antisyphilitic treatment.

Tertiary lesions of the **liver** are *fairly* common, either as perihepatitis, cirrhosis, gumma, or a combination of these conditions. They may be accompanied by a *remittent type of fever, and in the* tropics a gummatous liver may be diagnosed as abscess. *Subsequent* shrinkage may cause considerable *portal obstruction. As a* late result of syphilis the liver may become amyloid.

The rectum.—Tertiary lesions occur as local gummata, or as diffuse submucous infiltration. **Gummata** are found more often in women as round, elastic submucous swellings which vary in size from a pea to an orange. They may break down and lead to recto-vaginal fistula, which starts a severely ulcerative process tracking out into the ischio-rectal fossa. **Diffuse infiltration** is analogous to the nodular syphilide. It causes the mucous membrane to become stiff and inelastic, and numerous ulcers form. The ulceration spreads upwards and leads to considerable narrowing of the passage. *There is pain and tenesmus, with the passage of a foul discharge.* Examination discloses the ulcers with their well-defined edges. Sometimes the anus is surrounded by a ring of prominent, soft, fleshy growths radially arranged and flattened by mutual pressure, looking like cockscombs

Diagnosis of tertiary syphilis of the rectum.—The presence of a discharge and the discovery of ulcers just within the rectum should lead to an inquiry as to syphilis. *Tuberculous ulcer* is more *irregular and undermined;* the patient is tuberculous, and the Wassermann reaction may be negative. *Carcinoma* gives rise *to a* hard, irregular growth pressing into the bowel, which quickly becomes adherent to *other structures. The discharge is dark, and the ulcer* bleeds easily when palpated; the Wassermann reaction may be *negative.*

Gummata of the breast are comparatively rare. They appear as one or a number of round elastic tumours, the skin over which is at first freely movable. If a gumma comes to the surface, the skin becomes reddened, adherent to the tumour, and, breaking eventually, gives rise to a gummatous ulcer of the usual type. Gumma differs from *scirrhus* in its tendency to soften, rather than harden, in the centre, in the absence *of pain, and in reacting quickly* to anti-

syphilitic treatment. *Diffuse* gummatous infiltration causes uniform enlargement and hardening of the breasts. The enlargement is comparatively painless, and reacts well to antisyphilitic treatment.

Gumma of the brain occurring as a definitely circumscribed tumour is far less common than diffuse gummatous meningitis. It appears primarily in the membranes, which become matted together, and extends along the pial sheaths into the brain. It may occur anywhere in the brain, but favours the base, especially the optic chiasma and the interpeduncular space, and comparatively frequently the 3rd nerve and the arteries of the circle of Willis are involved. When it starts on the convex surface it favours the frontal and parietal lobes. The symptoms depend largely on the situation, and are most diverse. Generally, they are those of intracranial pressure, arteritis with resulting loss of function of the nerve centres or tracts served, and irritation and destruction of nerve tissue by direct pressure. In some cases localizing signs, such as limited paralyses or Jacksonian epilepsy commencing in one area of the body, may indicate the site of the lesion; in others, the skull is tender to percussion over the gumma; in yet others, the real nature of the trouble is discovered only on post-mortem examination.

Gumma of the spinal cord is very rare. It arises in the meninges, and is diagnosed by localizing symptoms of irritation and paralysis. Very rarely a gumma may grow from the periosteum of a vertebra and give rise to pressure symptoms.

PROPHYLAXIS

In a classical experiment on man, Metchnikoff prevented the development of syphilis, after inoculation with virulent syphilitic virus, by rubbing 25-per-cent. calomel ointment into the scarified area an hour after inoculation. A monkey rubbed with the same ointment twenty hours after inoculation developed syphilis. Subsequently the following formula was recommended:—

Calomel	33
Lanolin	67
Vaselin	10

In another experiment syphilis was prevented in a monkey by rubbing the inoculated area with the ointment eighteen hours after inoculation. It would not be safe, however, to rely on this experiment in the case of man, as monkeys are less susceptible to syphilis than men Metchnikoff and Roux considered watery solutions useless for the prevention of syphilis. Their conclusion seems to be based on an experiment in which mercury perchloride solution as

strong as 1 per cent. was applied; but perchloride of mercury in such a strength would produce a hard coagulum of the secretion on the surface, through which the disinfectant could not penetrate. Probably the most effective method would be to steep the part for some minutes in a 1-in-2,000 solution of biniodide of mercury and then rub in the above ointment. I have seen many failures from the use of such antiseptics as potassium permanganate, and even lysol, applied thoroughly a few minutes after exposure.

The prevention of accidental infection of fingers, lips, and other extragenital parts resolves itself into measures to prevent the direct, or almost direct, contamination of abrasions with the virus from syphilitic persons who are in the earlier stages of syphilis. Such persons should be warned of the risk arising from their sharing of table utensils, crockery, and house linen with others. They should not kiss others nor talk directly into people's faces, and articles which they have used should be dipped into very hot water. A further precaution is to keep open lesions smeared with an antiseptic ointment such as that of Metchnikoff.

Recently a fair amount of evidence has accumulated to show that the injection of an arsenobenzol compound such as is described below will prevent the development of syphilis. The evidence rests most strongly on cases in which patients who had been exposed to infection by intercourse with persons presenting early syphilitic lesions of the genitals have been injected with an arsenobenzol compound and have escaped infection, while others exposed almost at the same time have developed syphilis. The dosage differs from one dose of 0·3 grm. of "606" or 0·45 grm. of "914" to three or four doses at intervals of three days to a week. Naturally one would favour repeated dosage in such cases, since a partial destruction of the virus would be almost a worse evil than allowing the disease to develop.

The prevention of transmission to offspring resolves itself virtually into preventing infection of the mother. A man who has contracted syphilis should be advised to wait for at least four years before marrying; by that time the risk of transmission by sexual intercourse has usually disappeared, whatever the treatment. The period can be shortened by treatment, but if so, this must be prolonged and thorough. A syphilitic woman may convey the disease to her offspring long after she has ceased to be a danger through sexual intercourse. Efficient treatment of the mother before or during pregnancy will often prevent transmission of the disease, or, if it has already been transmitted, will go far towards curing the infant before it is born. Naturally, the earlier this treatment is begun, the more likely is it to be successful.

TREATMENT

The remedies most commonly employed for the treatment of syphilis are preparations of arsenic, mercury, and iodine. Arsenic and mercury are believed to destroy the parasites; iodine, to stimulate the tissues to clear away granulomatous tissue.

Recently, **bismuth compounds** have been announced as having a powerful antisyphilitic action. R. Sazerac and C. Levaditi, following up the discovery of Sauton and Robert that bismuth has a preventive and, to a certain degree, a curative action in hen spirillosis, conducted some experiments on animals infected with syphilis and with trypanosomiasis, injecting them with compounds of bismuth. The result showed that bismuth has a powerful effect in causing disappearance of *Sp pallidum* and of syphilitic lesions in animals. The *effect on trypanosomiasis was not so great. Subsequently they tested* tartro-bismuthate of potassium and sodium on human syphilis with equally promising results. Fournier and Guénot confirmed these results in 110 cases of syphilis treated with intramuscular injections of tartro-bismuthate of potassium and sodium in an oily suspension. *Sp pallidum* usually disappeared after the first or second injection; primary lesions healed in from six to twenty days, and secondary and tertiary lesions were almost equally rapid in disappearing. The effect on the Wassermann reaction did not appear to be quite so strong as that of the arsenical preparations. The dosage employed was 0 20 grm every two days, or 0 30 grm. every three days, the interval being increased, or the dose diminished, later in the course. A total of 2 5 grm. was given in a course lasting three weeks or a month The only side-effect noticed was some stomatitis, which called for reduction of dosage. The writer has insufficient experience of this new remedy to judge of its merits, but in two cases treated at St. Thomas's Hospital the results seemed to bear out the statements of the French authors. As will be shown below, mercurial and arsenical preparations have certain cumulative toxic effects which may make it difficult to continue their use in a given case to the extent necessary to cure the disease. If the claims made for bismuth are substantiated, it will be possible to alternate the remedies so as to leave perfectly safe intervals between courses of any one type, and so avoid late toxic effects.

Arsenical preparations.—"606," or dioxydiamidoarsenobenzol dihydrochloride, was produced by Ehrlich in 1909 It is now sold as salvarsan, arsenobenzol (Billon), arsenobillon, kharsivan, diarsenol, arsphenamine, and a number of other names, according to the country of origin and the manufacturing firm. It is a yellow powder which forms an acid solution when dissolved in water. Addition of an

alkali to this solution causes a precipitate which redissolves on addition of more alkali. Being *liable to change on exposure to air*, it is sold in sealed ampoules containing weighed amounts of the compound. At first it was injected *subcutaneously*, but there was too much local reaction, and it is now administered intravenously. It may be prepared for injection as follows:—

1. Inspect the ampoule to see that it is intact.
2. Dissolve the contents in fairly hot, *germ-free, metal-free distilled* water at the rate of 0·1 grm. in 10 c.c. of water contained in a tall, stoppered glass cylinder, which is shaken *until solution is complete*.
3. Add 0·8 c.c. of 4-per-cent. sodium hydrate solution for every 0·1 grm. of the remedy. *The solution becomes at first generally turbid and then perfectly clear.*
4. Add 0·5-per-cent. sodium chloride solution to make the strength not greater than 0·1 grm. in 25 c.c.
5. Test with litmus as a check on the correctness of *the above technique*.
6. Strain through sterile muslin or many layers of gauze.
7. Administer intravenously after it has stood for 5–10 minutes.

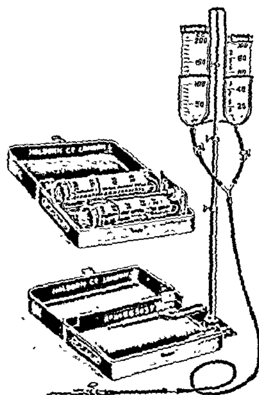


Fig. 105.—Portable "606" apparatus.

Owing to the large volume of fluid to be injected, a special apparatus is necessary. This may be a syringe by which the solution is alternately drawn from a receptacle and forced into the vein; or a bottle from which the solution is forced along a flexible tube to the needle by pumping air into the bottle above the solution; or the solution is allowed to flow by gravity from a funnel held above the patient. *My own preference is for the gravity method. It is advisable*, after inserting the needle, to allow a little saline to flow first, *as a precaution against the injection of "606" into the tissues should* the needle have happened not to enter the vein. Some saline should also be run in afterwards to clear the needle of the "606" solution. For this purpose it is convenient to contain the "606" in one funnel

and the saline in another, both funnels being slung side by side and connected, about a foot below, by a glass V-piece. After the needle has been inserted, the clip controlling the saline is opened, and as soon as it is seen that the flow is satisfactory the "606" solution is turned on, while the saline is shut off. The saline is turned on again as soon as the dose of "606" has flowed down the tubing, in order to sweep that remaining in the tube into the vein. A convenient form of apparatus is that illustrated in Fig. 195, as it can be packed in the case which forms the stand.

As "606" was inconvenient to administer, Ehrlich experimented to discover a compound having the same therapeutic properties but free from this drawback. The result was seen in two preparations, one of which, "914," produced shortly after "606," is now used very extensively, while the other, **sodium-salvarsan,** is "606" already converted to the disodium compound. The latter is a yellow powder which requires only to be dissolved in water, and can be given much more concentrated than the original preparation. It is about two-thirds the strength of salvarsan and, in equivalent doses, is more easily tolerated.

Ehrlich's first improvement of salvarsan, **"914,"** or dioxydiamidoarsenobenzol-monomethylene-sulphoxylate of soda, is now sold as neosalvarsan, novarsenobenzol (Billon), novarsenobillon, neokharsivan, novarsan, and neoarsphenamine. It is a yellow powder (containing 18–22 per cent. of arsenic) which is much more liable than salvarsan to become toxic on exposure to air, so that it must be administered very quickly after the ampoule has been opened and its contents have been dissolved. It forms a neutral solution in water. The most usual method of administration is the intravenous. The dose, from 0·45 to 0·9 grm. for adults (which corresponds to 0·3–0·6 grm. of "606"), is dissolved in 2–5 c.c. of distilled water and drawn into a syringe. The syringe is armed with a fairly fine needle, and the point of this is inserted into the vein, which should be distended as tightly as possible by fastening an elastic band round the upper arm and making the patient grasp a roller bandage. A pull on the piston causes blood to flow back into the syringe, showing that the needle is properly within the vein. The rubber band is released, the hand opened, and the piston pressed steadily home. The preparation can also be given intramuscularly, or into the deep subcutaneous tissues. Its therapeutic effect when administered intramuscularly or subcutaneously is undoubtedly greater than when given intravenously. The injection may cause considerable pain, which may be immediate, or may come on two or three days later and may last for about a week.

Recently a preparation, known as **sulfarsenol,** in many

respects similar to "914," has been synthesized. Its great advantage is that it can be injected subcutaneously with *very little* discomfort to the patient. It is a yellow powder which is readily soluble in distilled water and can be injected in a concentration of 0·6 grm. per c.c of water. It may also be dissolved in glucose solution (4·75 per cent. containing 0·5 per cent. phenol). It may be injected intramuscularly in the upper and outer quadrant of the gluteal region, or just over the fascia covering the glutei, as follows: In the upper and outer quadrant of the gluteal region the skin and fat are pulled away from the underlying fascia, by grasping them with the thumb and fingers of the left hand, and a 2-in. Record needle is entered obliquely at the base of the pyramid thus produced. The needle is made to under-run the fat so that its point may scrape on the fascia overlying the gluteal muscles. The charged syringe is fitted to the needle, and the injection given fairly slowly. The site is then massaged with a pad of lint.

Another preparation, introduced by Mouneyrat, and known as **galyl,** or tetraoxydiphosphaminodiarsenobenzol, is a greenish-grey powder which is soluble in alkali, and is sold in sealed ampoules already mixed with sodium carbonate, so that it is ready for intravenous administration when the contents of the ampoule have been dissolved in about 5 c.c. of distilled water. Galyl is also sold dissolved in glucose solution for intramuscular injection.

Two preparations have been introduced by Kolle, the successor of Ehrlich. One, called **sulfoxylate,** or **"1495,"** is a stable arsenobenzol preparation put up in ampoules already dissolved and ready for injection. The other preparation, known as **silbersalvarsan** is a combination of sodium-salvarsan and silver; it is an emery-coloured powder which forms a dark-brown solution in water. It is well to dissolve it in 8 c c. of water and, after puncturing the vein, to draw about 2 c c. of blood into the syringe. The injection should be given much more slowly than neosalvarsan, otherwise the patient may suffer from vaso-motor symptoms as noted below. When the vein is a very difficult one it may be better to inject in more dilute form, with a funnel and rubber tubing, as used for the administration of salvarsan or its substitutes.

Therapeutic properties of arsenobenzol preparations.—All the arsenobenzol preparations mentioned above act much more rapidly than mercury, and there is no doubt that their use has considerably improved the treatment of syphilis, though the first hope of Ehrlich that he had discovered a remedy which would cure with one dose has not been fulfilled. The greater certainty of cure is shown by the fact that unequivocal second [illegible] of syphilis, formerly a great rarity, are now comparativel[illegible] Kolle's silver salvarsan

appears to be about twice as powerful in immediate therapeutic effect as "606" and "914," and can consequently be given in much smaller doses. Sulfoxylate is slower in action. In permanence of effect the arsenobenzol compounds differ somewhat. Of the three better-known preparations, "606," "914," and galyl, experience indicates that, in equivalent doses, *administered intravenously*, the permanence of effect is in the order given. When the results of an intramuscular or deep subcutaneous course of neosalvarsan are compared with those of an intravenous course of any of these compounds, there is little doubt that the advantage rests with the intramuscular or subcutaneous method, and it is reasonable to expect that the same will be found in the case of the closely similar preparation, sulfarsenol. Enough is not yet known of silver-salvarsan and sulfoxylate to indicate their position in regard to permanence of effect, but the silver preparations appear to be valuable in severe ulcerative conditions of syphilis and in syphilis of the nervous system.

All these remedies have a certain toxic effect on the tissues, which is manifested in a small proportion of cases by symptoms described below. On the whole, "606" appears to give rise to immediate side-effects in a larger proportion of cases than the others. As a practical result, patients have to be kept under observation for some hours after salvarsan injections—a precaution which is not, as a rule, necessary after injections of the other remedies. The choice of preparation depends on circumstances. Other things being equal, the worker would probably choose "606" for routine intravenous, and sulfarsenol or neosalvarsan for subcutaneous treatment, because of their superior therapeutic effect, though it is possible that these may be ousted later by the silver combinations when these newer remedies have been sufficiently tested. But '606" has disadvantages in the complexity of its preparation, in the length of time consumed over the injection, and in the fact that the patient has to be detained for some hours; while "914" is simply prepared, and the patient can usually be sent away at once. Silver-salvarsan is not quite so convenient as "914," but sufficiently so for out-patient work For subcutaneous treatment sulfarsenol is at present the remedy of choice

Toxic effects of arsenobenzol remedies.—These compounds all tend to damage capillary endothelium. In patients who have died as a result of overdoses, or of idiosyncrasy, there have been found blockage of cerebral capillaries, with small hæmorrhages around these; hæmorrhagic "nephritis"; hæmorrhage into lung capillaries; submucous petechiæ and ecchymoses in the stomach and bowel; and, in a comparatively few cases, degeneration of liver cells amounting to a condition like that found in acute yellow atrophy.

Clinically, toxic effects are manifested by one or more of the symptoms enumerated below. The list is a comparatively long one, but most of the symptoms are so mild, infrequent, or preventable as not to preclude the routine use of these remedies. In roughly chronological order they are as follows:—

1. *During or immediately after the injection:—*
   (1) Vaso-motor disturbances, also known as anaphylactoid symptoms or minor nitritoid crises. (2) Urticaria. (3) Syncope. (4) Pain in the gums and teeth.
2. *Following the injection usually by a few hours,* and occurring generally on the same day:—
   (5) Rigor, rise of temperature, and headache. (6) Vomiting, diarrhœa, pain in the back and cramp in the legs. (7) Herpes (labialis or zoster).
3. *At various times from a day or two to a month or longer* after a single injection or a course of injections:—
   (8) Albuminuria. (9) Stomatitis. (10) Chronic headache; lassitude; loss of appetite, weight, and sleep. (11) Erythema and dermatitis. (12) Jaundice. (13) Severe cerebral symptoms.

1. *The vaso-motor symptoms.*—The face becomes flushed, and the tongue and lips may swell; there may be respiratory distress, and the patient may become unconscious. Often a severe attack is followed by more or less generalized *urticaria.* As a rule the symptoms last for about half an hour, but in rare cases recovery is not complete for a number of hours Some patients are peculiarly susceptible. In others the symptoms may be produced by imperfect preparation of the remedy for injection or too rapid administration, as they depend on the physical state of the solution on entering the circulation.

As measures of prevention, solutions of "606" should be well alkalized and given dilute; solutions of "914" should not be given concentrated if the preparation does not dissolve perfectly in practically its own weight of water; sodium-salvarsan and silver-salvarsan, if given in concentrated solution, should be injected slowly. The treatment usually employed is to inject 10–15 min. of adrenalin chloride (1 : 1,000) hypodermically.

Syncope is usually mental in origin, unless it precedes vomiting. *Pain in the gums and teeth* is probably vaso-motor. The *peculiar taste in the mouth* of which some patients complain during the injection is a very common symptom when concentrated solutions of "914" are given, but does not accompany injections of silver-salvarsan.

2. *Rigor, rise of temperature*, and *headache* are very rarely severe, but are commoner after first than subsequent injections. *Diarrhœa* and *vomiting* are not frequent unless there has been an error in technique, or the patient has been indiscreet in his dietary. Quite often they are followed by *herpes*. *Usually these symptoms have all disappeared by the next day.*

3. *Albuminuria* very rarely causes any anxiety. *Stomatitis* is not often attributed to arsenobenzol remedies, but they seem to increase the tendency to this complication which is manifested by patients on mercurial treatment.

Chronic headache, lassitude, etc., are symptoms of intolerance displayed by a few patients, and indicate the necessity for a rest from treatment.

Various *skin affections* may occur besides the urticaria and herpes mentioned above, and may be very serious. The mildest is some slight itching which quickly passes off. Some patients show a transient and limited erythema, but in a small minority a punctiform erythema quickly spreads over the body, is accompanied by most intense itching, and often then passes on to a condition like pityriasis rubra. There is extensive exfoliation of the epidermis and localized weeping eczema. The constitutional symptoms are severe, with fever, insomnia, and loss of appetite, and there may also be severe diarrhœa, perhaps with jaundice, indicating intestinal catarrh. The incidence of dermatitis depends largely on the intensity of the treatment. Generally speaking, a male adult of average build will easily tolerate 2·6 grm. of "606" in doses of 0·3–0·5 c.c. spread over a period of 57 days, but if this period is shortened the percentage of dermatitis increases noticeably. A careful watch for signs of skin irritation will often supply timely warning of the idiosyncrasy and, by preventing the administration of more arsenobenzol, will save the patient from a severe attack. The treatment of exfoliative dermatitis following arsenobenzol injections is often troublesome on account of the generalized exfoliation and the local pustulation and eczema. Usually, the patient should be in bed and well protected. An intramuscular injection of intramine 2·5 c.c. will often abort a commencing erythema, as also will bleeding to a pint. Internally, quinine, 5 gr. every four hours, and ichthyol, 5 gr. in capsule night and morning, are useful, and the bowels should be regulated with paraffin. The diet should be simple, containing large quantities of bland liquids, and should not include eggs and meat. Locally, calamine lotion and starch poultices are soothing. An occasional bran bath is valuable, but careful precautions should be taken against chill, as these patients are very prone to pneumonia. For weeping surfaces I prefer 10-per-cent. ichthyol ointment.

Jaundice following injections of arsenobenzol preparations appears to have become much more common in recent years, and a voluminous literature on its etiology has accumulated in all countries without any definite consensus of opinion having been attained. In the very great majority of cases the type is mild, with clayey stools and high-coloured urine. Occasionally it is much more severe, with epigastric and hepatic pain, restlessness and delirium, followed by death. Broadly, the changes found in these rare cases have been extensive degeneration of liver cells with round-celled infiltration of the supporting connective tissue; multiple subserous hæmorrhages, and frequently hæmorrhages into lung alveoli. Either type may occur during a course of injections, or be delayed for many months afterwards. In respect of the delay in onset, as in some other features, the fatal type of jaundice strongly resembles trinitrotoluene poisoning. The exact part played by arsenobenzol in the production of jaundice is also uncertain, but the weight of evidence seems at present to favour a connexion between the amount of arsenobenzol administered as routine in a given time and the proportional incidence of jaundice, the more concentrated the course the higher being the percentage of jaundice. Recent work appears to indicate that the liver which is empty is more likely to take up arsenobenzol than the charged liver, and it has been suggested that a measure of prevention may be to keep the patient well fed on carbohydrates. It is agreed that fats should be avoided.

The treatment of both types of jaundice mentioned above consists in milky diet without meat or eggs, and large doses of bismuth subcarbonate and sodium bicarbonate, with regulation of the bowels by paraffin.

Severe *cerebral symptoms*, with headache followed by mental confusion, epileptiform convulsions and coma, ending in death in a large proportion of cases, are now very rare, and I was able to discover only eight cases among soldiers treated in Britain before and during the War. Such cases were much more frequent in the early days of salvarsan, when it was common for two injections of 0 6 grm. to be given with an interval of forty-eight hours, and there can be no doubt that the comparative infrequency of cerebral side-effects among cases treated in military hospitals has been due to the moderate initial dosage employed and the spacing out of the injections. One patient, whom I saw comatose, was restored within half an hour by phlebotomy to the amount of 20 oz, the removal of 15 c.c. of cerebro-spinal fluid, and the injection of 1 c.c. of adrenalin chloride, 1 in 1,000. Other workers have been equally successful by this means. The treatment should be applied at once, and the lumbar puncture should be repeated if the symptoms continue.

Jarisch-Herxheimer reaction.—The immediate effect of these as of other antisyphilitic remedies is to increase the intensity of the syphilitic process. This may be important when an artery supplying a vital organ is already partly blocked; then the temporary increase in the severity of the process may result in a complete blockage which may be disastrous, as when the patient develops hemiplegia, or dies of obstruction of the basilar artery. Such cases are very rare; I have seen only one which gave reason for alarm on this account, that of a patient who developed hemiplegia after the third injection; treatment was continued, on my recommendation, and the patient recovered completely.

Neuro-recurrences—Though not strictly a direct effect of arsenobenzol treatment, paralysis of various cranial nerves, especially the 7th and 8th, became more common shortly after its introduction. These phenomena have been proved to be syphilitic recurrences, and their greater frequency at one time was due to the fact that many patients were treated with one or two doses only, in the belief that that was sufficient to cure. It seems probable that the arsenobenzol remedies prevent the development of spironemes in the skin and mucous membranes more easily than in the central nervous system, and that the absence of any general skin and mucous membrane reaction results in failure of development of immune substances which would keep the spironemes in the central nervous system in check. If this is so, the physician clearly must administer an amount of treatment which will ensure the destruction of spironemes in the central nervous system as well as the other tissues. If he stops short of this he may give an opportunity to the spironemes in the brain and spinal cord to set up greater trouble than would otherwise be possible.

Precautions—In sufferers from advanced Addison's disease, bleeders, and those on the point of death from severe visceral disease, the arsenobenzol compounds are contra-indicated.

In all cases where intravenous injections are employed it is advisable for the patient to have a saline purge on the morning of each injection. The stomach should be empty, as otherwise the intravenous injection has an emetic action, but previous fasting should probably not be too prolonged, otherwise the empty liver cells may take up the arsenobenzol and be poisoned by it.

In visceral disease of a less severe type than that mentioned above, in alcoholism, and when the patient is prone to such skin affections as eczema and severe seborrhœa, it is advisable to begin with a dose of 0·1–0·2 grm. of "606" or 0·15–0·3 grm. of "914," and to increase the intervals in the outline of treatment given later (p. 814). The same applies to patients suffering from syphilis of the

brain, cord, or viscera when there is reason to fear an exacerbation of the process.

In all cases the commencing dose should be moderate—0 3 grm. of " 606 " or 0 45 grm. of " 914 " for an adult male who is otherwise healthy. The intervals between doses should be spaced in a way which has proved to result in a very low proportion of toxic side-effects. I have found in the case of men that, when 2 6 grm. " 606 " is compressed into less than a 57-day course, the incidence of such toxic side-effects as dermatitis increases noticeably. The patient should be watched carefully throughout the course for signs of intolerance. This precaution may not absolutely prevent severe side-effects, but such as do develop will usually be much milder than when no notice is taken, for example, of an erythema and the treatment is continued to the end of the course.

Mercurial preparations.—Mercury was formerly the sheet-anchor in the treatment of syphilis. Its action is much slower than that of the arsenobenzol compounds, and, when it is used alone, relapses are frequent while the patient is actually under treatment. The great advantage of mercury is that it can be kept almost continuously in the circulation, so that the action is maintained after the dose of arsenobenzol has been excreted until it is safe to administer another arsenobenzol injection. To ensure the certain destruction of all the parasites, it seems to be necessary that an antisyphilitic remedy should be present constantly in the body fluids for a period of many months. That one dose of arsenobenzol, even a large one, does not cure syphilis is now well known. It seems probable that the organisms most deeply placed in infiltrates are not reached and that, before the last one can be destroyed, the infiltrate must be removed and the area revascularized. Such a process takes time, and whilst it is occurring it is necessary that the parasites should be kept in check as they become exposed; otherwise they would be set free to start the process of syphilization anew. This conception indicates the rôle of mercury in the modern treatment of syphilis. If, however, the view is held that the disease is not cured by one dose of arsenobenzol because the parasites are in a resistant form, it is equally reasonable to hold that, as they resume the form which is susceptible to attack by antisyphilitic remedies, one of these ought to be present in the tissues to keep them in check; and it is mercury that can most conveniently be maintained in the tissues for this purpose.

Methods of administration.—The *oral method* is much favoured, but is apt to cause gastro-intestinal disturbance and is exposed to the risk of failure through the patient's forgetfulness. I employ it only when the patient cannot take injections or inunctions, and also

when, a large amount of arsenobenzol and mercurial treatment having been given, the patient cannot continue injections or remain under close observation. Favourite preparations are: (1) hydrargyrum cum creta, 1–2 gr ; (2) hydrargyrum iodidum viride, $\frac{1}{6}$–$\frac{1}{4}$ gr.; (3) hydrargyri perchloridum, $\frac{1}{6}$ gr.; (4) hydrargyrum tannicum oxydulatum, 1 gr.; (5) pil hydrargyri, 1–3 gr.; (6) liq. hydrargyri perchloridi, $\frac{1}{2}$–1 dr., often prescribed in a mixture with potassium or sodium iodide. The first five of these are usually given in pill form, often combined with a little opium, e.g. pulv. ipecacuanhæ composita, 1–2 gr., with hydrarg. cum cret., and extractum opii $\frac{1}{6}$ gr. with the others, to counteract the irritant effect. It is a good plan to ring the changes on these preparations until one is found which does not upset the patient. Generally speaking, the best plan is to give courses of a month or six weeks, gradually increasing the daily intake of mercury until slight signs of stomatitis appear, and then reducing the dose. After the first and second course a rest of a week is given, and at the end of the third the interval is one month, after which the series of three courses is repeated. The length of time over which this treatment is prolonged depends greatly on the amount and character of the previous treatment.

Inunction.—This is a most valuable method of administering mercury, but must be carried out by a skilled rubber, and has the inconvenience of soiling the skin and clothes. On successive days 5–10 grm of 33$\frac{1}{3}$-per-cent. mercurial ointment is rubbed for twenty minutes into thighs, calves, arms, chest, and back, a bath being taken on the sixth day and the cycle restarted on the seventh. The number of rubbings varies from 60 to 200 in a course, the length of a course depending on the patient's tolerance, which is judged by the state of the gums, the weight, and the general well-being.

Intravenous injections are rapid in effect but very apt to give rise to toxic symptoms; they appear to me to have the further disadvantage that the effect is not sustained. The usual preparations employed are the cyanide and the perchloride, in doses of 1 c.c. of the 1-per-cent. solution, daily or on alternate days, to a total of twenty or thirty.

For *intramuscular injections* both soluble and insoluble preparations are employed. Among the *soluble* preparations are the biniodide (1-per-cent. solution) in doses of 1 c.c, the bibromide, the benzoate, and the perchloride, the perchloride being made up as follows:—

Sod. chlor.	gr. iv.
Aq. destill.	ℳ 400
Dissolve, filter, and add hydrarg perchlor. . .	gr. viii.

Dose, 5–10 min.

brain, cord, or viscera when there is reason to fear an exacerbation of the process.

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Sod. chlor	gr. iv.
Aq. destill.	♏ 400
Dissolve, filter, and add hydrarg. perchlor. . .	gr. viii.

Dose, 5–10 min.

The soluble preparations are more rapid in effect, but this is not sustained. They have the further disadvantage of having to be given daily or on alternate days.

The *insoluble* preparations most commonly employed are mercury in fine subdivision, calomel, and mercury salicylate. Suspensions of these remedies ready for use are sold by most chemists. The doses usually employed are: Mercury 1–1½ gr., calomel ½–¾ gr., salicylate 1½–2 gr. Calomel causes more pain than the other two preparations, and my own preference is for mercury in fine subdivision. The advantages of the insoluble preparations are that, on account of the slow absorption, enough mercury can be given in one injection to last a week, and that the effect is sustained.

The *technique* of intramuscular injections is simple. The site usually chosen is the upper and outer quadrant of the gluteal region. A needle 2 in. long is introduced, almost to its full length, perpendicularly to the skin surface. The base is examined to see that no blood is oozing from it, the syringe is applied, the piston pulled upon to see that the needle is still not within a vein, and the piston is then pressed home. The needle having been withdrawn, the site is well massaged with a ball of cotton-wool. Before an insoluble preparation is drawn into the syringe, the suspension should have been well mixed, either by stirring with a glass rod or by energetic shaking of the bottle.

Toxic effects of mercury.—These are stomatitis, nephritis, colitis, general malaise, and dermatitis.

Stomatitis can usually be prevented with care. The patient's teeth should be set in order before beginning the course, and he should brush them night and morning. Potassium chlorate is useful, and may be incorporated in the dentifrice. If the gums become sore, the mercury must be stopped and more energetic treatment applied to the mouth. Lozenges of potassium chlorate to suck, and swabbing with peroxide of hydrogen, followed by the application of collosol argentum, or of a mixture of liq. arsenicalis 1, vinum ipecacuanhæ 1, and spiritus vini rectificatus 2, usually suffice to restore the gums to a healthy condition. An astringent mouth-wash should be employed, and sulphur taken internally.

Nephritis seldom results from the moderate doses of mercury now employed, but the irritant effect of mercury on the kidneys should be remembered in cases where these organs are already diseased. Arsenobenzol preparations also tend to cause nephritis, so that, in certain cases, it may be advisable to withhold one preparation during the period when the other is being administered.

Colitis is extremely uncommon as the result of the ordinary mercurial course of treatment. *General malaise* is apt to result from

pushing mercury too freely, and it is always advisable to keep a close watch on the patient's weight and general condition. *Dermatitis* as a result of mercurial treatment alone is very rare, but since arsenobenzol treatment tends to act in the same direction it may be advisable, when there is reason to suspect that the skin is susceptible, to withhold the mercury whilst arsenobenzol is being administered.

Iodine preparations promote the resolution of syphilitic processes, and are most useful in the later stages. The tissue reaction is qualitatively the same in all stages, however, and as there are grounds for supposing [illegible] ds to bury the parasites, making then [illegible] remedies, there is reason for the emp [illegible] in all stages. Usually I have given them for short periods between courses of treatment by arsenobenzol and mercury, on the principle of preparing the ground for the further action of the more definitely specific remedies. The favourite preparation is potassium iodide, in doses of 5–30 gr. thrice daily. If it cause gastro-intestinal disturbance, even when given very dilute in water, it will be better tolerated if made up in a cent.-per-cent. solution and the dose dropped into milk. The depressing effect of potassium iodide is neutralized by giving it with nux vomica. When potassium iodide is not well borne it may be replaced by sodium or ammonium iodide. Many proprietary preparations are advertised as superior to potassium, sodium, and ammonium iodides, but they should be reserved for cases where the older preparations cannot be tolerated.

General management of syphilis.—The main principles to be observed in the treatment of syphilis are—

(1) To begin as early as possible, before the parasite has become buried in the sclerosed primary sore or entrenched in comparatively inaccessible regions, such as the central nervous system.

(2) To continue as long as experience shows that there is a possibility of the patient relapsing if treatment ceases.

(3) To exploit the patient's natural resistance by maintaining his general health in the highest possible condition.

Since the decision as to cure has to be postponed in all cases for some years after suspension of treatment, and relapse cases are particularly difficult to cure, it is better to treat all cases as if they were of the resistant type, even at the risk of over-treating some. Too much reliance is placed at present on a negative Wassermann reaction as an indication for suspension of arsenobenzol treatment, and I do not believe in continuing only with mercury after the reaction has become negative. Mercury is a slowly-acting, comparatively feeble antisyphilitic agent, and if arsenobenzol remedies had not come into

use it would have been found that the two-years' treatment formerly considered sufficient in this country would long ago have been prolonged to four or five, as in other countries. The modern preparations of "606" and "914" are by no means equal to the original ones in therapeutic activity, and this applies particularly to "914," the preparation most commonly employed. For these reasons it is necessary to continue the treatment far longer than until recently was considered sufficient.

In all cases of primary sore it is of the greatest importance to apply local treatment to destroy the organisms *in situ*. Otherwise they may escape the remedies circulating in the blood. It may be possible to remove the sore by circumcision, or to destroy it with a cautery. Failing this, the sore may be rubbed with 30-per-cent. calomel ointment.

The following are the courses which are being given at the St. Thomas's Hospital V.D. Treatment Centre to men of average build in different stages of syphilis. For women who are not pregnant it may be advisable to reduce the dosage according to weight.

ROUTINE TREATMENT OF ADULT MALE SYPHILIS CASES

1. Primary Cases with Negative Wassermann

	Days of Treatment	Potass. Iodide Grains t.d.s	Mercury Intra-muscular Grains	"914" (or) Intravenous or Intra-muscular Grammes	Sulfarsenol (or) Sub-cutaneous Grammes	Silver-salvarsan Intravenous Grammes
	1			0·45	0·48	0·15
	8		i.	0·45	0·48	0·15
	15		i.	0·45	0·48	0·15
	29		i.	0·60	0·60	0·20
	36		i.	0·60	0·60	0·20
	50		i.	0·75	0·60	0·25
1.	57		i.	0·75	0·60	0·25
	58—64	v				
	65—71	vii				
	72—77	x				
	78		i.	0·75	0·60	0·25
	85		i.	0·75	0·60	0·25
	92		i.	0·75	0·60	0·25

Blood-test on 92nd day.

2. 93—126 Rest.
3. 127—147 Potassium iodide as 58—77.
4. 148—239 Repeat treatment as from 1st to 92nd day.
5. Suspend all treatment, but test the blood every three months.
6. At end of one year test blood after provocative injection of "914."
7. During second year test blood every six months.
8. At end of second year test blood after provocative injection.

II. Primary Cases with Positive Wassermann

Days of Treatment

1. 1—239 As in I. 1—4. Blood-test on 92nd day of each course.
2. 240—307 Rest.
3. 308—329 Potassium iodide as in I. 1.

		Mercury	"914" (or)	Sulfarsenol (or)	Silver-salvarsan
		Grains	Grammes	Grammes	Grammes
4.	330	i.	0·60	0·60	0·20
	337	i.	0·60	0·60	0·20
	344	i.	0·60	0·60	0·20
	358	i.	0·75	0·60	0·25
	365	i.	0·75	0·60	0·25

5. Suspend all treatment and continue blood-tests at intervals as in I. 5—8.

N.B.—This programme is based on the assumption that at the end of the first 10 injections the Wassermann reaction is negative. If the reaction is positive after the tenth injection, proceed as laid down below for cases with secondary signs.

III. Cases with Secondary Clinical Signs

Days of Treatment

1. 1—365 As in II. 1—4. Blood-test on 92nd and 365th days.
2. 366—433 Rest.
3. 434—455 Potassium iodide as in I. 1.

		Mercury	"914" (or)	Sulfarsenol (or)	Silver-salvarsan
		Grains	Grammes	Grammes	Grammes
4.	456	i.	0·60	0·60	0·20
	463	i.	0·60	0·60	0·20
	470	i.	0·60	0·60	0·20
	477	i.	0·75	0·60	0·75
	484	i.	0·75	0·60	0·75

5. Suspend all treatment and continue blood-tests at intervals as in I. 5—8.

IV. Later Cases with Active Symptoms

Days of Treatment

1. 1—57 1st course of 7 injections as in I. 1.
2. 58—77 Potassium iodide as in I. 1.
3. 78—147 Rest.
4. 148—182 Course of 5 as in II. 4
5. 183—203 Potassium iodide as in I. 1.
6. 204—336 Repeat 78—203.
7. 337—469 Repeat 78—203.
8. 470—567 Rest.
9. 568—602 Course of 5 as in II 4.
10. 603—623 Potassium iodide as in I. 1.
11. 624—749 Rest.
12. 750—784 Course of 5 as in II. 4.

Before treatment is suspended both blood and cerebro-spinal fluid should be negative. After it is suspended the patient is put under observation, being examined clinically once a month and by blood-test every three months for a year. At the end of the year both blood and cerebro-spinal fluid are examined a week after a provocative injection of, say, 0 45 grm. of "914." During the second year the blood-tests are applied at intervals of six months, the provocative injection and examination of cerebro-spinal fluid being repeated at the end. As a rule, it is not advisable to allow a patient to marry until four years have elapsed from infection and he has remained free from all signs, clinical and serological, for at least two years following suspension of all treatment.

Pregnant women, in the early months, may receive the course mentioned above from the 1st to the 57th days, " 914 " being employed and the dose not exceeding 0 6 grm. On account of the susceptibility of the kidneys, it is advisable to withhold mercury for the first few injections until it is seen how the injections are tolerated. Following on this course, potassium iodide is given for two weeks, and the arsenobenzol and mercurial course repeated after two months. On this principle, treatment may be continued almost to the end of pregnancy, a careful watch being kept on the kidneys throughout.

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CONGENITAL SYPHILIS

By BREVET-COLONEL L. W. HARRISON, D.S.O., K.H.P., R.A.M.C. (RET.)

Definition.—Syphilis due to infection of the fœtus *in utero.*

General course.—The chances of a sufferer from acquired syphilis transmitting the disease to children depend generally on infection of the mother. Once a woman becomes infected, there is practically no limit, apart from treatment, to the period of time, within the child-bearing *period, during which she may continue to* give birth to syphilitic infants. Infection of the mother generally depends on the age of the disease in her consort. The risk of conveying *the disease by sexual intercourse is greatest during the first* two years, and is slight after about the fifth, though cases have been recorded of men conveying the disease to their consorts considerably later than this. *Infection of the child directly by the sperm, the* mother escaping, is a question on which there is no consensus of opinion, but cases have been recorded which support it fairly strongly. Such a case is that related by J. Whitridge Williams (*Bull. Johns Hopkins Hosp.*, xxxi., 335, 356), in which a woman bore a series of healthy children to her healthy husband both before and after one which was a twin, by superfœtation, with a syphilitic, *the result of* intercourse with a syphilitic lover. The mother remained apparently healthy, with a negative Wassermann reaction throughout, but it is recorded that the apparently healthy twin died. *Cases* have been reported of women bearing a series of syphilitic infants to one husband and healthy ones to a subsequent one, but women may cease to bear syphilitic children to the same syphilitic *husband.* Other cases supporting purely paternal transmission are those where treatment of the husband resulted in healthy children, but these may have been similar coincidences. *The strongest evidence against* sperm infection is the fact that the mother of a congenital syphilitic cannot acquire syphilis from the infant (Colles's law). The high proportion of such mothers who give a positive *Wassermann reaction* has led some authors to explain Colles's law by the assumption that the mothers are syphilitic already.

If a healthy mother is infected more than seven months after

conception the infant usually escapes, but it may acquire syphilis in birth through the infected maternal passages, or later from the mother's secretions. The date of infection of the fœtus is unknown, but possibly varies, and it may be that, if the mother's disease is recent, the earlier the fœtus is infected the less are the chances of its maturing. As will be shown, a large proportion of syphilitic infants born alive do not show symptoms for some weeks after birth. It has been suggested by Rietschel that, in these cases, infection may have occurred only towards the end of pregnancy, when the uterine contractions tore open the sinuses and gave a free path to the virus. This would explain the fact of the Wassermann reaction being often negative at birth. On the other hand, the infection may be so mild in the child that it is discovered only by accident, and it seems more likely, in these cases, that, although it may have occurred early in the life of the fœtus, it was small in amount and largely neutralized by the mother's protective substances. This would explain the tendency of the disease to be milder and milder in successive children

The question of transmission is considerably affected by treatment, and it can be said with confidence that congenital syphilis is a most preventible disease.

The consequences of infection of the fœtus vary in different cases from early death, followed by abortion of a macerated fœtus, to so mild an effect that adult life is reached without the occurrence of any clinical manifestation. The number of cases seen in which a congenital infection is discovered in the adult by accident compels the belief that many with inherited syphilis go through life without the disease being discovered. Between these wide limits the disease shows all degrees of severity.

Generally speaking, the more recent the infection of the parents the more severe the disease in the fœtus and the more likely its death, either *in utero* or very shortly after birth. The classical history of the syphilitic family is that of a series of miscarriages followed by premature births of diseased infants who died very quickly; next, infants born alive at term who showed signs of disease either then or a few weeks later, and died or struggled through with difficulty; then infants who displayed little or no evidence of syphilis in the early months, but developed late lesions between the age of five and puberty, then children in whom the only evidence throughout life was a positive Wassermann reaction with, perhaps, an isolated clinical sign on some damaged part of the body; and lastly, perfectly healthy children. This, however, is by no means always the course of events, since apparently healthy children may be preceded and followed by those who are diseased, and it may even happen

that one of twins may appear healthy and the other show pronounced signs of syphilis.

An approximate idea of the effect of congenital syphilis on fœtal and early infantile life may be gathered from the statistics collected by workers who have studied the histories of families in which syphilis was known to exist in one or more members. Veeder found that, in 100 families, 331 pregnancies resulted in 40 per cent. of stillbirths or infants who died very soon after birth, 15 per cent. who died later in infancy, 35 per cent. who survived but were syphilitic, and only 10 per cent. apparently healthy. Jeans and Butler compared 100 families in which one or more children were being treated for non-syphilitic contagious disease with 100 selected at random and a similar number of syphilitic families, and found as follows:—

Group	*Total pregnancies*	*Deaths before birth*	*Born living, now dead*	*Total*	*Percentage loss*
Contagious diseases (non-syphilitic)	444	46	70	116	26
Random selection	442	42	59	101	25
Syphilitic	453	116	104	220	46

Harman compared 150 families in which syphilis was known to have been transmitted with a similar number of families of the general population of the poorest classes. The results were as follows:—

Group	*Pregnancies*	*Abortions and miscarriages*	*Stillbirths*	*Born living, but died in infancy*	*Alive but syphilitic*	*Percentage loss*
Syphilitic ..	1001	92	80	229	210	40 05
General ..	826	61	17	94	—	20 80

These figures show an agreement with Jeans and Butler's which is very close, considering that they are derived from different countries The proportion of pregnancies in the syphilitic families which failed to produce a living child in Jeans and Butler's statistics was 25 6 per cent, and in Harman's, 17·1 per cent. Harman's figure is similar to the 20 7 per cent. of 1,132 pregnancies of syphilitics collected by H. C. and M. H. Solomon, and contrasts with Harman's 9 1 per cent. failures among the pregnancies of the general population, with Jeans's

9 7 per cent. of 886 pregnancies, and with Duke's 7·7 per cent. of 5,808 pregnancies According to these calculations, syphilis in the parents approximately doubles the chances of a pregnancy failing to produce a living child. It is interesting in this connexion to note that H. C. and M. H. Solomon found the average birth-rate of 555 syphilitic families to be 2 05, with average living children 1 62, against an average of 3 8 per family of the general population of the same part of the United States—New England. An analysis by Whitridge Williams showed that in 10,000 consecutive deliveries, 26 per cent. of the fœtal and infantile deaths between the seventh month and two weeks following delivery were the result of syphilis, but these included both negroes and whites. In a subsequent analysis of 4,000 deliveries it was found that 12 out of 99 such deaths among whites and 92 out of 203 deaths among blacks were due to syphilis.

If an infant is born alive it may suffer from a bullous eruption, which is present at birth or appears within a few days, and is of bad omen. More commonly signs appear from three to six weeks after birth, in the form of eruptions which are similar in general characteristics to those seen in the early and recurrent phases of acquired syphilis. Jeans's studies showed that the first clinical symptoms appeared in the first two months in 81 per cent. of cases. Gummata of the skin may also appear in the early months of infancy. Mucous-membrane lesions manifest themselves in the well-known snuffles and the child's hoarse, raucous cry. Partly from the nasal obstruction and partly from actual disease of bone, the bridge of the nose may become depressed and various degrees of deformity of the nose follow. Often within the first six months, syphilitic disease of the testicle develops. In many cases the bones are affected within the first year, a common form being an epiphysitis which results in syphilitic pseudo-paralysis. Besides this, signs of osteitis may appear in such bones as the tibia and the phalanges, producing characteristic deformities. Changes in the skull, late closure of the fontanelles, parietal and frontal bosses causing the "hot-cross bun" cranium and protruding forehead, are often seen in syphilitic infants, but may be due to coincident rickets. Thinning of the cranial bones, especially the occipital (craniotabes), is sometimes found, but may also be the result of rickets Premature arrest of the expansion of the cranial bones with early closure of the fontanelles causes microcephalic idiocy. Choroiditis, retino-choroiditis, and iritis may occur in the very early months, though they are commoner after about the seventh year. Blindness may result from intracranial disease. The infant may be deaf from syphilitic otitis media, or from intracranial destruction of the auditory nerve. Studies of the cerebro-spinal fluid have shown that the central nervous system is very frequently involved in congenital syphilis, so that it is

not surprising that symptoms dependent on meningeal and cerebral disease should be sometimes seen. Besides blindness and deafness, already mentioned, convulsions may result from syphilitic meningitis, and it is easy to understand how congenital idiocy may often be due to syphilis, a supposition which is confirmed by the high proportion of congenital idiots who give a positive Wassermann reaction. The viscera suffer more profoundly in congenital than in acquired syphilis, and white pneumonia and severe hepatic disease are often found in infants who die early. The spleen is frequently enlarged, and in many cases there is severe anæmia with considerable wasting, which produces the wizened, old-man look seen in severe cases. The connexion of congenital syphilis with congenital deformities, or with congenital disturbances of the endocrine functions, has not been established Holt failed to obtain a positive Wassermann reaction in 56 consecutive infants suffering from such congenital malformations as spina bifida, congenital heart disease, and hare-lip. Browning, on the other hand, found 17 out of 25 cases of congenital heart disease with a positive reaction, and Findlay and Robertson, 7 out of 11. *It is easy to understand how such a disease as syphilis*, which invades every part of the body, may interfere with the full development of structures, either by destruction of the cells composing them *or of those which provide the stimulus to cells to complete the structures* which it is their function to build.

If the first year is survived it is uncommon for further signs to *appear before about the fifth year. Between then and puberty* a certain proportion of congenital syphilitics develop late manifestations which may affect any part of the body, but are classically seen in the *Hutchinsonian triad—notching of the central incisors, inter*stitial keratitis, and deafness from labyrinthine disease. Besides these phenomena, syphilitic arthritis is not uncommon; some of *the children suffer from tertiary ulceration of the skin; osteitis of* various bones sometimes occurs, and ulceration of the palate and fauces may result in severe scarring and perhaps perforation of the palate *Visceral disease, especially of the liver, heart disease*, paroxysmal hæmoglobinuria, and juvenile tabes or general paresis are other possibilities which in childhood or adolescence menace those *who have inherited syphilis Generally, in fact, it can be said that* there is no organ or structure which may not be invaded and destroyed, or its functions severely impaired, by syphil[illegible]ecially when the *invasion occurs in the beginning of the* [illegible], and that [illegible] which are not[illegible]ined on other

middle age before one or other of these later signs appears, and it is often then an interstitial keratitis which develops in an injured eye, or perhaps some ulcerative skin lesion.

Infants suffering from hereditary syphilis seem to be more prone than others to develop rickets, and some authorities believe strongly that syphilis *per se* predisposes to rickets. In this case, however, as in the supposed greater predisposition to tuberculosis, the cause may lie merely in the profound interference by syphilis with the general nutrition of the infant.

Whether a congenital syphilitic can transmit the disease to the third generation is a question which is often debated. Cases have been recorded in which the evidence seemed very strong, but transmission to the third generation must be rare. It must be remembered that a person who has inherited syphilis may acquire it, though this also is a rare event; such a person could easily transmit his acquired infection, and the case might then be recorded as an instance of transmission to the third generation. Again, it seems sometimes to be forgotten that a person with congenital syphilis may marry one with acquired. Perhaps more likely than the transmission of syphilis to the third generation is the propagation, by those suffering from hereditary syphilis, of children with various malformations and dystrophies

Morbid anatomy.—The changes in the placenta due to syphilis vary considerably. In well-marked cases the placenta is larger than normal and œdematous, owing to arteritis leading to extensive thrombosis. The substance is more friable than usual, and has a mottled appearance on section. The stroma and epithelium of the villi show inflammatory proliferation, and there is round-celled infiltration. It is easy to understand how the above changes in a severe degree interfere profoundly with the nutrition of the fœtus and lead to its early death, apart from infection of the fœtus itself *Spironema pallidum* is by no means always found in sections, but has been demonstrated in the walls of the large vessels, in the mucoid tissue of the villi, or in contact with the capillary walls. The changes enumerated are found in varying degrees in the placenta in cases of miscarriage a few months before term, in stillbirths, and in cases where syphilitic infants are born alive. On the other hand, examination of the placenta may reveal no evidence of disease, though later events prove the infant to be syphilitic. The cord may be considerably thicker than normal, with much thickening of the vessels, but the changes are not pronounced in fœtuses which survive to the end of pregnancy.

The macerated fœtus of an early abortion shows nothing characteristic, but the changes in those born dead, or who die within a few weeks of birth, are usually very emphatic, and indicate the extent

to which the tissues are invaded. The *lungs* may show peribronchial infiltration with fibrosis, and alveoli filled with desquamated cells, the organs being large, with white patches of hepatized tissue. These changes may be associated with numerous miliary gummata, but isolated gummata of larger size are not common. It is possible, as Still suggests, that fibroid disease with bronchiectasis, sometimes seen in later childhood, may be syphilitic.

The changes in the *heart* have been carefully studied by Warthin, who believes that cardiac disease is far more common in congenital syphilis than is generally believed. *Sp. pallidum,* he says, may be found in large numbers in the intermuscular spaces and occasionally within the fibres, without any noticeable change in the tissues. *On the other hand, the heart-muscle* may degenerate in places, becoming converted into fibrous tissue, or undergoing fatty degeneration, atrophy, or necrosis. In necrosis the tissue elements are pushed apart "and the spaces filled with a fine albuminous precipitate, a mucoid substance, and cells." These parenchymatous changes may exist without interstitial ones, but the latter are also present in most cases. *The interstitial changes are primarily vascular or perivascular,* at first with proliferation of capillaries, followed by extensive thrombosis All stages between a mucoid œdema and fibrosis are found in different areas. In addition, localized myxoma-like formations may be seen containing large numbers of *Sp. pallidum.* The cases in which Warthin found purely parenchymatous lesions were mostly virulent congenital and active secondary and early tertiary syphilis; in milder and older infections the interstitial changes predominated He states that *Sp. pallidum* may be found in the heart when none can be discovered elsewhere in the body.

The *liver* must be affected to a greater or less degree in most cases. The changes are most pronounced in those born prematurely and those who die shortly after birth. In these the condition is one of hypertrophic cirrhosis with perihepatitis. The organ is considerably enlarged and its margins are rounded. The surface is smooth and strewn with numerous white dots, like semolina grains. Microscopically is found an intercellular infiltration with fibrosis, the liver cells being separated by round cells and fine strands of new-formed connective tissue. The changes are especially evident around the vessels, the coats of which are considerably thickened and their calibre reduced. *Sp. pallidum* may be found in huge numbers throughout the liver. Cellular collections give rise to miliary gummata. Such profound changes as these are incompatible with life. Isolated gummata are sometimes found in older children either during life or after death, and Still suggests that the multilobular cirrhosis found in later childhood may sometimes be syphilitic in origin.

The *spleen* is very commonly though not invariably enlarged, and may be fibrosed. The enlargement is due partly to portal obstruction and partly to cellular infiltration. Isolated gummata in later childhood are very uncommon.

The *kidneys* show varying degrees of parenchymatous degeneration and interstitial nephritis. As in acquired syphilis, liver, spleen, and kidneys may become lardaceous in later cases.

The *intestines* may be the seat of miliary gummata which sometimes ulcerate through the mucous membrane.

The *long bones* often show characteristic changes at their epiphysial ends, where the line of calcification can be seen with the naked eye to be broadened. According to Heubner, the change can be seen as early as the fifth month of fœtal life, and is most marked in the lower end of the humerus and radius, and upper end of the tibia, and at the costo-chondral junctions. At the junction of the cartilage with the bone the cartilage cells proliferate, but become degenerated and fatty owing to compression of the vessels. The process may go on to softening and separation of the epiphysis. Local and diffuse periostitis also occurs, and is described in more detail later (p. 831).

The *central nervous system* may show all the changes found in acquired syphilis—pachymeningitis and leptomeningitis, with miliary and isolated gummata, infiltration of cranial nerves, and generalized and local arteritis, leading to death of the centres supplied. In later childhood parenchymatous degeneration resulting in general paresis, tabes, or tabo-paralysis may supervene.

The above are the main changes found in congenital syphilis and the tissues in which they occur, but no structure is safe from invasion by *Sp. pallidum*, with resulting embarrassment or destruction of its function by direct action of the virus, by compression from cellular infiltration and fibrotic changes, or by interference with its nutritional supply from narrowing or thrombosis of its vessels.

The **Wassermann reaction** may be negative at birth, possibly because the infection is too recent for the reaction to have developed. The reaction is almost always positive in those with clinical symptoms, and is often particularly difficult to abolish by treatment. This is especially the case when the reaction is positive in later childhood and adolescence. In this respect congenital syphilis does not differ from acquired syphilis of long standing. On the other hand, there is considerable evidence to show that the reaction tends to die out after puberty, though in many cases it is probably maintained throughout life.

The cerebro-spinal fluid shows pathological changes in over 40 per cent. of cases in early infancy.

Skin lesions.—**Syphilitic pemphigus** is not a common event in congenital syphilis and is usually of bad omen when coincident with birth, or occurring a few days afterwards. The eruption consists of bullæ which become pustules, resting on dark-red bases and affecting chiefly the palms and soles. The pustules break quickly, leaving brownish-red, slightly eroded surfaces covered with crusts, or with half-dried tags of epidermis.

Diagnosis.—The eruption is distinguished from *pemphigus neonatorum* by appearing earlier than the non-specific affection, by its occurrence on the palms and soles, by the dark-red bases of the lesions, by the presence of *Sp. pallidum* in the secretions, and by the wasted condition of the infant, which contrasts with the well-nourished state in pemphigus neonatorum.

The **maculo-papular eruption** is the commonest rash in congenital syphilis, and usually appears from three to six weeks after birth. The macules are red or reddish-brown discs which may be generalized on the trunk and limbs, but are commonest on the napkin area, about the nose and mouth, on the palms and soles, on the genitals, between the buttocks, and in the flexures. The colour is more intense than in acquired syphilis, and the spots are often annular, as in the recurrent syphilide of adults. In places which are much exposed to pressure and irritation, as on the buttocks, palms and soles, the spots run together into roundish areas which are glazed, dull-red, and tend to scale rather profusely, especially on the palms and soles. Adjoining such areas typical macules are usually to be found, and help to dispel any doubt as to the diagnosis. In moist areas, such as the flexures, moist papules are common, as in acquired syphilis. Between the buttocks and at the upper and inner sides of the thighs the papular eruption may take the form of broad condylomata. Papules on the palms and soles may be raised into minute pin-head blisters which subsequently show lamellar scaling. The eruption may be pustular or even bullous in places. At the angles of the mouth and below the lower lip, fissures are fairly common, and the scars which they leave, radiating from the angles of the mouth, are a valuable sign of syphilis in later years.

Diagnosis.—The chief diagnostic characteristics are the early appearance of the symptoms, within a few weeks of birth, the palmar and plantar lesions of typical appearance, the polymorphism of the rash and its association with such signs as snuffles and possibly cachexia, the presence of *Sp. pallidum* in the secretion of the moist lesions, the positive Wassermann reaction, the mother's history of repeated miscarriages of macerated fœtus, and the history of other members of the family.

Other rashes which may be mistaken for the maculo-papular

eruption of congenital syphilis are ordinary erythemata, impetigo, seborrhœic dermatitis, and vacciniform dermatitis. Ordinary *erythemata* are brighter and found mostly on parts which are rubbed with wet clothes and napkins, but not on the palms or soles, nor in the flexures. *Impetigo* is not associated with other signs characteristic of syphilis, and at the margin of a confluent lesion which might cause confusion are usually found impetiginous lesions of typical appearance. The affection may be found in another member of the family. *Seborrhœic dermatitis* is a more superficial lesion. It causes circumscribed patches covered with greasy scales. *Vacciniform dermatitis* is rare. It causes vesicles and sharply defined excoriations or ulcers $\frac{1}{4}$–$\frac{1}{2}$ in. in diameter about the genitals. It is not associated with other signs suggestive of syphilis.

Gummata of the skin may make their appearance during the first year or be deferred until considerably later, just as in the acquired form. The syphilitic furuncles of Barlow are gummatous nodules varying in size from a pea to a walnut, which break down and discharge their contents through central openings. Other gummatous skin lesions are similar to those seen in the acquired form. Occasionally gummatous ulcers become phagedænic and result in considerable destruction of the affected part.

The **diagnosis** of gummatous skin changes rests on the history and on typical appearances simulating those met with in acquired syphilis.

The **nails** usually show changes coincidently with the early eruption In the acuter forms the nail is raised on a bed of seropus, which escapes from under the pinkish-red sides. In the milder form the nail loses its lustre and becomes narrow at the base and irregular. Unless treatment is instituted, the nail is usually shed and replaced by one with similar appearances.

The **hair** of the scalp may be shed more or less extensively, especially over the back and sides, and loss of the eyebrows is very suggestive of syphilis On the other hand, the hair may be unusually abundant at or shortly after birth, so much so that this condition has been spoken of as the "syphilitic mop" It is a sign which occurs apart from syphilis, and is of no diagnostic value in the absence of other signs.

The **mouth** may be occupied by mucous patches similar to those found in acquired syphilis. At any age after the subsidence of the early rash, gummatous infiltration may lead to perforation of the hard or the soft palate Ulceration of the pillars of the fauces, the soft palate, and the posterior pharyngeal wall, similar to that sometimes seen in the later stages of acquired syphilis, may occur fairly early in childhood, or be delayed until well on in adult life. Scars

are left, with deformity of the parts, which may later be valuable evidence of congenital syphilis when other stigmata are absent. Glossitis with leucoplakia and gummata of the tongue similar to those of the acquired form are sometimes seen.

The **teeth** may show valuable evidence of congenital syphilis. Those most frequently and characteristically affected are the upper central permanent incisors; more rarely the lower central incisors show the same features The affected teeth are widely separated from one another and from their neighbours, have wider bases than cutting edges, and the corners of the cutting edges are rounded off, while the centre of the cutting edge is occupied by a crescentic notch

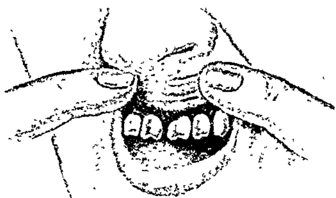


Fig. 196.—Upper teeth of a woman the subject of congenital syphilis. (*After Hutchinson.*)

Teeth with these characters are *Hutchinsonian teeth* (Fig. 196), and are diagnostic of congenital syphilis. By no means all congenital syphilitics show Hutchinsonian teeth, and in any case they tend to lose their characters after the age of 20, so that the absence of typical teeth should not weigh against a diagnosis of congenital syphilis. Hutchinsonian teeth should not be confused with *hypoplastic teeth*, the result of illnesses in infancy. Hypoplastic teeth are pitted and irregular, but not peg-shaped and notched. They certainly occur in congenital syphilitics, but are also due to many other diseases of infancy. *Moon's teeth* are dome-shaped first molars, the central part of the crown having failed to develop and the sides having fallen together; they are diagnostic of congenital syphilis.

Rhinitis is an early sign of congenital syphilis, giving rise to the well-known snuffles of the classical case. The discharge may be

very little in amount and mucous in character, or abundant and purulent or mucopurulent, and sometimes stained with blood. The discharge, like others from the early lesions of infants suffering from congenital syphilis, contains *Sp. pallidum* abundantly and is highly contagious. In severe cases the chronic obstruction, with resulting negative pressure within the nares, results in some sinking of the nasal arch, and "saddle-nose" remains as a permanent stigma of the disease. The same causes operate in producing the highly arched palate frequently seen in congenital syphilis. Destruction of the nasal bones results in a more severe degree of sinking of the nasal arch. Gummatous ulceration of the nasal floor may lead to perforation of the hard and soft palate, which may occur at any time from the age of 2 years to adolescence or later.

Laryngitis is manifested by the infant's hoarse cry. In severe cases there may be ulceration of the larynx, leading to interference with respiration, and even to suffocation. In later childhood and in adolescence gummata may occur similar to those seen in acquired syphilis.

The lungs.—Infants who are stillborn or die of syphilis shortly after birth may have one or both lungs affected with the white pneumonia of Virchow. Localized gummata are occasionally found, and fibroid changes may occur in late infancy, so that in children chronic symptoms referable to the lung should always be investigated closely with syphilis in view.

The **heart** is comparatively seldom found diseased in life, but interstitial myocarditis is occasionally discovered post-mortem, as well as localized gummata. Warthin's studies referred to above would suggest a greater frequency of heart disease than is commonly believed, and he suggests that it may account for sudden death in apparently healthy children

The connexion between syphilis and congenital heart disease is uncertain. It is significant that these cases give a high proportion of positive Wassermann reactions (De Stefano found 27 positive out of 32), and it is possible that here, as in other malformations, *the virus may have interfered with the destiny of the group of cells* ordained to build up the structure

Vascular lesions play a prominent part in all the manifestations of congenital syphilis.

The **intestines** suffer frequently from multiple gummatous ulcers, and the resulting gastro-intestinal disturbance contributes to the general malnutrition.

The **liver** is commonly found to be diseased in those cases which die *in utero*. In infants who are born alive, symptoms of liver disease may develop during the first few months, manifested either as

diffuse interstitial hepatitis or as definite gumma. In the former case, the liver is moderately enlarged, smooth, and perhaps a little firmer than usual. There may be jaundice or, more rarely, ascites. Gummata are usually multiple. They are not generally recognized *in early infancy*, but in later childhood, say from the age of 6, may be felt as multiple bosses on the surface of the liver.

The **spleen** is very frequently enlarged, and *the enlargement* may be very pronounced. The part played by syphilis in the causation of splenic anæmia is uncertain.

The **kidneys** are liable to show the same changes as in the acquired affection, and cases of parenchymatous as well as of interstitial nephritis have been reported from the age of a few weeks to 18 years It has been suggested that this affection may have some relation to the chronic interstitial *nephritis which is sometimes found* in children and young adults.

By some authorities **paroxysmal hæmoglobinuria** is said to be sometimes the result of congenital syphilis, and they claim that **Raynaud's disease,** which is so commonly associated with this affection in adults, may very often have the same foundation.

The **testicles** may be affected at any time from the age of a few weeks to adult life. Syphilis is practically the only cause of testicular enlargement before the age of 5 months. The enlargement may be diffuse or nodular, and causes no pain, so that it is often overlooked. Later the affected testicle shrinks considerably and becomes fibrotic, so that, in an adolescent, or an adult, a considerably *shrunken testicle without previous history of disease or injury* is very suggestive of hereditary syphilis.

The testicles may be normal in consistence but fail to increase in size, so that in adult life they are still infantile.

The **bones** are very frequently affected, and the changes produced often remain as stigmata which are valuable signs of congenital syphilis.

Epiphysitis can be demonstrated in many stillborn infants at the lower end of the femur, and radiographs of syphilitic infants often show a line of enlarged calcification at the epiphyses of the long bones. If the process develops, the epiphyses may become separated. Any long bone or rib may be affected, but especially the lower ends *of the humerus and radius, the upper end* of the tibia, and the ribs at their costo-chondral junctions. The bone becomes thickened at the epiphysial line. There is rapid loss of movement, with acute tenderness, so that the infant screams when the limb is moved. The condition is known as the "pseudo-paralysis of Parrot." Sometimes *suppuration follows and* the joint becomes infected with secondary organisms.

Diagnosis.—The chief distinguishing characteristics of syphilis of the bones are the early onset, within the first three months, and often the first four weeks, the presence of other signs of syphilis, and the family history.

Barlow's disease and *infantile paralysis* appear later than the third month. In Barlow's disease there is diffuse thickening of the diaphysis, contrasting with the localization at the epiphysial line in syphilitic epiphysitis. In infantile paralysis the muscles will not contract when the skin is pinched. In all of these there are, naturally, collateral signs which assist the diagnosis.

Dactylitis is often an early manifestation, occurring before the end of the second year, though even in congenital syphilis it may be delayed until adult life. The symptoms and diagnosis are described in the article on acquired syphilis (p. 794).

Periostitis of the long bones usually occurs between the ages of 8 and 14, and affects a number of bones, often symmetrically. The affection may be localized, producing bosses, for example, on the diaphyses of the arm bones, the tibia, the ribs, or the clavicle, or enlargement of the ends of the same bones. Sometimes these localized gummata break down, and the result is spontaneous fracture or a discharging sinus with considerable deformity of the bone.

Diffuse periostitis may affect any bone, and usually leads to considerable thickening. There may be a fusiform enlargement extending from the articular end for some distance along the diaphysis and simulating a sarcoma, from which it is distinguished by the history and by its more definite outline in a radiogram. More commonly the whole diaphysis is greatly enlarged. This change is seen most characteristically in the tibia, which becomes considerably increased in its antero-posterior diameter, while the crest is curved with its convexity forwards. The whole bone looks as if its sides had been flattened, and the general appearance is that of a sabre-scabbard. Occasionally the bone may break down at one or more spots, and a sinus form.

Syphilis of the **flat bones** has been partly dealt with in connexion with the nose and palate. Sometimes there may be definite necrosis of the skull, with possible exposure of the dura mater, and the process may be multiple. Swellings on the front of the sternum have also been recorded as due to congenital syphilis. These bone affections are all usually found within the first year In many cases of congenital syphilis bosses form on the frontal and parietal bones around the anterior fontanelle, giving the top of the cranium the "hot-cross bun" appearance (Fig. 197). The forehead may bulge unduly, presenting a marked convexity when viewed from the side

These 100 cases were those admitted to a children's hospital, so that the numbers cannot be taken as a true index of the proportion of cases of congenital syphilis which develop nervous symptoms in the general population.

Many authorities had long held that congenital syphilis has a great deal to do with a number of the nervous affections met with in childhood and young adult life, but proof was difficult because often the available histories are very vague and signs of syphilis are absent from the bodies of many of the patients. By means of the Wassermann test it has now been shown that an important proportion of these cases are syphilitic—far more, in fact, than show the stigmata or give a clear history of syphilis. The question cannot further be discussed here, but it may be added that idiocy, hemiplegia, with other paralyses (including those of individual cranial nerves), and hydrocephalus have frequently been connected definitely with congenital syphilis Thus Kate Fraser and H. E. Watson found a positive reaction in 44 9 per cent of 89 abnormal children (10 epileptics with imbecility, 2 congenital imbeciles, and 77 feeble-minded). In 15 out of 34 cases of epilepsy, with or without mental defect, the reaction was positive, as it was in 4 out of 10 epileptics without mental defect. Gumma of the brain and meninges also occurs, while juvenile tabes and general paralysis are, of course, syphilitic in origin.

The eyes.—Harman found congenital syphilis responsible for over 30 per cent. of blindness in 1,100 school children. Interstitial keratitis accounted for 191 cases, and was associated with iritis in 73 and choroiditis in at least 30 (in many the condition of the cornea could not be determined owing to opacity of that structure). Iritis without other signs was present in 6, cataract in 14, and optic atrophy, with or without disseminated choroiditis, in 125

Choroiditis and **iritis** often occur in the early months, having been found as early as the first day Choroiditis gives rise to a number of areas of inflammation, imparting to the fundus a crateriform appearance, the craters being white and surrounded by sharply pigmented borders. There are also opacities in the vitreous. Iritis appears to be milder than in acquired syphilis, but otherwise presents the same signs According to Hutchinson, it occurs most often at the age of 5 months, and may be unilateral or bilateral.

Interstitial keratitis occurs usually between the ages of 5 and 15, but may be delayed until considerably later in life. The cornea gradually becomes opaque *in a patchy manner, the opacity* spreading from the margin to the centre, and some patches being denser than others. Usually, after a few weeks, the other cornea begins to be similarly affected. After the opacity has existed for

some weeks the cornea becomes vascularized, with very fine vessels invading it, and the vascularization may be so dense that a pink patch is produced—the classical "salmon patch." In the course of the disease the cornea may be weakened and bulge before the intra-ocular tension, or it may become ulcerated. After remaining for many months, the opacity gradually clears, but some patches of opacity are often left in the cornea. There is usually a greater or less amount of iritis and choroiditis in addition to the keratitis, and as the amount of these cannot be gauged through the opaque cornea, it is wise to be cautious about the prognosis.

In another form, the greater burden falls on the iris and choroid, and the keratitis is more punctate in character. Opaque dots form at the back of the cornea, and these coalesce to a triangular patch of opacity in the lower segment. The signs of associated iritis are those of the plastic form already described.

In addition to the above diseases, the eye may be affected by cerebral syphilis, causing optic atrophy, hemianopsia, and paralyses of various branches of the 3rd nerve, with resulting strabismus.

Diagnosis.—The diagnosis of interstitial keratitis is not difficult when the above characters are considered with the history. Opacity of the cornea due to paralysis of the ophthalmic branch of the 5th nerve, *neuro-keratitis*, is distinguished easily by the associated anæsthesia of the cornea and temple, by the history of acquired syphilis, and by the characters of the cerebro-spinal fluid.

Almost all the eye diseases mentioned may be due to other causes, and the diagnosis rests largely on collateral signs of syphilis. Syphilis is so often the cause of eye disease that almost the first task in diagnosis is to search for other evidence of its presence in the patient.

The ears.—Congenital nerve deafness may be the result of central nerve syphilis or of syphilitic meningitis. **Otitis media** and **otorrhœa** may occur in connexion with the chronic rhinitis found in early infancy. They may be purely syphilitic, or complicated with pyogenetic infection. The discharge is highly infectious, an important fact to remember in dealing with these patients The whole middle ear and labyrinth may be destroyed, and the child become a deaf-mute

A serious consequence of congenital syphilis is the syphilitic affection of the **internal ear** which occurs between the ages of 7 and 20, and quickly leads to complete deafness without preceding symptoms. It is met with more often in females, the proportion being put by various authors at from two to four females to one male. It is frequently associated with keratitis, usually commencing rather later than the eye complaint. The onset is often rather sudden, sometimes with tinnitus and vertigo, but more commonly

without, and as a rule both ears become quickly affected, though one may be attacked before the other. The patient soon becomes hopelessly deaf. In other cases the deafness, though eventually as complete, is more gradual. This affection has been ascribed *variously* to (1) syphilitic meningitis extending to the nerve structures of the internal ear; (2) endarteritis and hæmorrhages (Baratoux); and (3) otitis media followed by para- and peri-labyrinthitis, or by invasion of the labyrinth through the foramen ovale. This last view is held by J. S Fraser and R. Muir, who have examined in detail a case which showed that the infection "invades the narrow spaces of the petrous and also *attacks the labyrinth capsule, giving rise to a chronic form* of osteo-myelitis which slowly invades the perilymph space of the labyrinth (gradual form of deafness)." They consider that the sudden cases are due to rapid invasion of the hollow spaces of the inner ear through the foramen ovale or the foramen rotundum causing syphilitic panotitis

Treatment.—In view of the length of time during which a *syphilitic woman may transmit the disease to her children, and the* uncertainty of tests of cure, the safest course is to treat her throughout each pregnancy, even though she may have received what is called thorough treatment on first infection Even when the treatment begins late, experience has shown that the results are eminently satisfactory, apparently healthy infants being born to a large proportion even of those mothers who conceive in the early stages of syphilis. *The chief dangers are abortion and nephritis, but these* can be avoided by care as to dosage and a close watch on the urine. The first dose should be 0 3 grm of "914," if the intravenous method is chosen, and this is increased to 0 45 grm. after a week. Thereafter, provided that no signs of intolerance are shown, the course is completed with six more intravenous injections of 0 45–0 6 grm. After an interval of eight weeks a course of five or six injections is given, *followed by another interval, and so on to a month from* the end of pregnancy. Either the intramuscular or the deep subcutaneous method of administering arsenobenzol is suitable for pregnant women, on account of the mildness of the general reaction to which it gives rise. Probably the best preparation for the purpose is sulfarsenol, since it causes very little discomfort, especially when injected just over the fascia covering the gluteal muscles. A good initial dose for *women of average build* is 0·36 grm., increased the following week to 0·42 grm.; then 0·48 grm., followed by about five injections of 0·6 grm. at weekly intervals. A suitable medium for solution of the drug for [illegible] injection is 50-per-cent glucose solution containing 1 per [illegible] used for each dose.

[illegible] mercury during the periods of

arsenobenzol treatment, giving it either as pills or by injections during the intervals.

Whether such treatment prevents the infection from passing to the fœtus, or is also treatment of the infected fœtus, is uncertain. This depends largely on the date when the fœtus becomes infected. In any case, in the present state of knowledge, it is safer to continue treatment of the infant after birth. Such treatment is assisted by continuing the mother's treatment and inducing her to nurse the infant, though her milk must be supplemented by remedies administered directly to the child

In the case of the infant, the combined treatment with mercury and one of the arsenical preparations has undoubtedly given the best results. The dosage of the arsenical preparation depends on the age and condition of the patient. For a child of one month a good initial dose is 0·05 grm. of "914," though Findlay recommends 0·1–0·15 grm. as quite safe for an infant of one to two months, increased to 0·2–0·3 grm., especially for the older children. For yet older children the dose is correspondingly increased. The courses of treatment should proceed on the same lines as those laid down for adults, the patient being regarded in the same light as one affected with acquired syphilis. As to the method of injection the practice differs. Findlay believes strongly in the intravenous route, choosing for young infants a scalp vein. The infant is wrapped tightly in a blanket, and a nurse holds the head firmly on the table whilst also applying a thumb to the temple to make the selected vein prominent. The operator works from above the child's head, using a No. 1 needle (with a needle which is very fine the vein is apt to be transfixed) Other workers inject into the external jugular, and a few into the superior longitudinal sinus The technical difficulties connected with intravenous injection of infants have influenced many in employing the intramuscular method, which does not appear, in the hands of those I have questioned, to make the infant fretful. The best method is to dissolve the dose in the smallest possible bulk of water, say 5 min, and inject into the gluteal region, as in adults. *Sulfarsenol* is probably the best remedy for the purpose, as it causes much less pain in adults than any other preparation on the market

The mercurial treatment may take one of many forms. *By the mouth:* liq. hydrarg. perchlor. 10 min, increased to 30 min., thrice daily in the milk; calomel in doses of $\frac{1}{16}$ to $\frac{1}{6}$ gr. thrice daily; or grey powder in doses of $\frac{1}{4}$ to $\frac{1}{2}$ gr. thrice daily, increased to 1 gr. thrice daily at a year old. Mercury by the mouth may cause diarrhœa; this can be avoided by combining it with pulv. cret. aromat, or with pulv. ipecac. co, the latter in doses of $\frac{1}{15}$ gr, increased to $\frac{1}{2}$ gr. at twelve months. *Injections* of soluble and insoluble preparations of

mercury into the muscles may be preferred. Mercurial cream in doses of $\frac{1}{6}$ gr., or the salicylate suspended in a fatty basis in doses of $\frac{1}{3}$ gr., may be given weekly during the period of the arsenical injections, or mercury perchloride in doses of $\frac{1}{50}$ to $\frac{1}{25}$ gr. twice or thrice a week. *Inunctions* may cause dermatitis, but have many compensating advantages in the treatment of infants. A piece of mercurial ointment the size of a pea is rubbed, as Findlay recommends, for fifteen minutes on successive days into the abdomen, back, each axilla, each groin, in turn, and back again to the abdomen. Between courses it is useful to administer syr. ferri iodidi, for the tonic effect and that of the iodine. The treatment should be prolonged over two years, as these patients correspond to the more advanced types of acquired syphilis, and it is important to do everything possible to prevent later manifestations.

The treatment of children and adults suffering from congenital syphilis should be carried out on the same principles as those laid down for adults in the late stages of syphilis, the dosage being calculated on age, weight, and condition.

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VENEREAL DISEASES OTHER THAN SYPHILIS

By C. A. LEEDHAM-GREEN, M.D., F.R.C.S.

Anatomy. The lumen of the urethra.—In the resting state the walls of the male urethra are in contact with each other, and are only separated during the flow of urine and semen, or the passage of a surgical instrument.

The diameter of the lumen, or, more correctly, the extent to which the canal may be dilated, varies greatly in its different parts. The relative dilatability of the various portions is shown in Fig 198, which is drawn from a cast of the urethra taken in fusible metal immediately after death. The prostatic and bulbous parts are more dilatable than the penile and membranous parts; the meatus is not only the narrowest, but by far the most resistant As will be seen later on, it is important to know precisely to what extent the several portions of the normal urethra can be dilated. This is indicated in the following table:—

			*French scale**
Meatus . . .	7 to 8 mm.	in diameter	= No. 21 to 24
Middle of penile .	10	„ „ „	= No 30
Bulbous portion .	13 to 15	„ „ „	= No. 39 to 45
Membranous portion	9 to 10	„ „ „	= No 27 to 30
Prostatic portion .	13 to 15	„ „ „	= No. 39 to 45

* I e. will admit a urethral instrument of this size.

Muscular fibres of the urethra and bladder.—Although it is convenient anatomically to divide the urethra into the several parts mentioned above, in practice the canal may be separated into two portions, the anterior and posterior This is no arbitrary division, but is founded upon an anatomical and physiological basis. The anterior portion comprises the penile and bulbous parts; the posterior, the membranous and prostatic. While the anterior portion is surrounded by erectile tissue, the posterior is enveloped by muscular fibres. Of these it is necessary to say a few words. Situated

within the prostate and surrounding the vesical orifice there is the internal prostatic or vesical sphincter, an ill-defined ring of involuntary muscular fibres intermixed with much elastic tissue. The fibres of this muscle are so slender that Finger and many other authorities believe that their action can be but slight, and insufficiently powerful to prevent the escape of the urine from the distended bladder. Within the prostate, below the internal prostatic sphincter, and separated from it by glandular tissue, is another and more powerful ring of muscular fibres, chiefly voluntary, which surrounds the urethral canal and constitutes the external prostatic or vesical sphincter. Where the urethral canal leaves the apex of the prostate, it is still surrounded by a thick layer of voluntary muscular fibres, known as the compressor urethræ (Fig. 199)

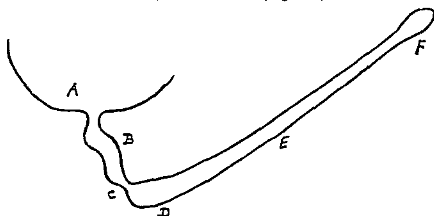


Fig. 198.—Cast of the male urethra.

A, Bladder, B, prostatic portion, C, membranous portion; D, bulbous portion; E, penile portion; F, fossa navicularis.

This last muscle plays a very important part in the production of "spasm of the urethra." A simple bougie, in its passage through the membranous portion of the urethra in a healthy person, stimulates the nerve-endings of the mucous membrane and causes contraction of the compressor urethræ muscle; it is therefore grasped and hindered in its passage towards the bladder. When the urethra is inflamed, the slightest irritation to the mucous membrane, such as is caused by the passage of urine, may give rise to so violent a spasm of this muscle as to cause retention of urine. This spasmodic contraction may be provoked not only by the passage of a foreign body like a bougie, but also by the pressure and irritation of fluids; thus even a non-irritating fluid injected up the healthy urethra is prevented from entering the membranous portion by the contraction of the compressor muscle. The spasm becomes still more marked when an astringent or irritating fluid is injected up an inflamed urethra.

It is true that under an anæsthetic, or by the adoption of certain measures which will be referred to later, it is possible to fill the bladder by injecting fluid into the meatus. But this in nowise contradicts the established fact that fluids injected with an ordinary gonorrhœal syringe do not usually pass beyond the bulbous urethra

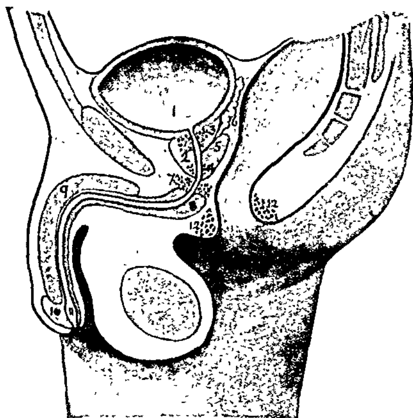


Fig. 199.—The male urethra and adjacent parts.

1, Bladder, 2, prostate gland, 3, internal vesical or prostatic sphincter, 4, external vesical or prostatic sphincter; 5 ejaculatory duct, 6, seminal vesicle, 7, compressor urethræ muscle surrounding membranous urethra, 8, bulb of the corpus spongiosum, 9, corpus cavernosum, 10, glans penis; 11, fossa navicularis; 12, sphincter ani

Now, just as the compressor muscle prevents the passage of fluids to the bladder, so it prevents fluids from passing the opposite way; therefore, if pus or blood be present in the urethra behind the compressor muscle, the fluid will tend to pass backwards into the bladder rather than forwards towards the meatus

This sharp separation of the urethra into an anterior and posterior portion by the compressor muscle is of the greatest importance for the

proper understanding of the pathology, symptoms, and treatment of *gonorrhœa*.

ACUTE URETHRITIS

This disease is caused by an inoculation of the urethral mucous membrane at the meatus with the gonococcus—the specific virus; it soon extends as an acute catarrhal inflammation as far as the bulb, but not, in favourable circumstances, beyond it. If the inflammation spreads beyond the bulb to the posterior urethra, this extension must be regarded as a distinct complication, bringing in its train new and unfavourable symptoms, and calling for a different mode of treatment.

ACUTE ANTERIOR URETHRITIS

Incubation.—The period of incubation between the inoculation with the virus and the appearance of the first symptom of the disease varies within certain limits. It may be as brief as one or two days, or it may extend to two or even three weeks; but in three-fourths of the cases it is confined within the limits of one week. Most commonly the first symptoms are noticed on the third or the fourth day. It rarely occurs that the period of incubation is less than two days. Instances recorded where the period of incubation is less than two days are generally to be explained as exacerbations of latent chronic gonorrhœa, and not as fresh infections

Symptoms.—Generally, the first symptom noticed by the patient is a slight burning or tingling sensation at the end of the penis, especially on micturition The lips of the meatus then become swollen, everted, and moistened with a slight, tenacious, mucous secretion, which rapidly becomes copious and purulent. During the next few days the pain on micturition increases considerably, so much so that the patient dreads to pass water. The discharge rapidly passes from clear mucus to muco-pus, and then to thick creamy yellow or greenish-yellow pus, which is secreted so profusely as to drop constantly from the meatus. As a rule, the penis is red and swollen, and the prepuce œdematous, so that the glans is uncovered with difficulty. Not infrequently the lymphatics of the organ are inflamed, and appear as thin red streaks in the integuments of the penis, and the lymphatic glands of the groin are swollen and tender.

Distressing sexual symptoms are seldom absent, the inflammatory irritation of the parts inducing increased sexual desires. In the earliest stages of the disease this condition often provokes the patient to sexual excesses; but, as the inflammation increases, all voluptuous feelings are lost in the intense pain which an erection of the inflamed organ evokes. These painful erections, often accompanied by seminal

emissions, form a characteristic feature of the most acute stage of the disorder, and seriously interfere with rest and sleep.

The inflamed condition of the urethra and the corpus spongiosum renders them less elastic than usual, consequently, when the penis becomes swollen and erect, it curves downwards, and the inflamed urethra can be felt as a cord holding down the penis; hence the term chorda venerea. At these times it not infrequently happens that the pus is tinged with blood which has escaped from the engorged capillaries of the urethral mucous membrane.

Considering the severity of the local symptoms, the general constitution is surprisingly little affected. Apart from slight pallor of the face, loss of appetite, a feeling of malaise, and sometimes, at the acme of the inflammation, a trifling rise of temperature, the general condition is hardly impaired. The symptoms usually increase in severity up to the second or third week, and then, if all goes well, gradually abate as the inflammation slowly dies down. The secretion becomes thinner, more mucoid, and lessened in quantity, until at length only sufficient remains to glue the lips of the meatus together It then disappears, so that at the end of the fifth or sixth week the entire process is over, and the disease is cured.

This may be regarded as the normal and most favourable course, but it is liable to many exceptions Apart from the occurrence of the special complications to which this disease is so peculiarly liable, and which are more conveniently discussed later in this article, the course of the disorder may be altered in the following ways: (a) *By an exacerbation or recurrence of the acute inflammation*; (b) *by an extension of the disease to the posterior urethra*, and (c) *by the inflammation passing into a chronic condition.* The first of these calls for little comment; the others must be considered in detail

Exacerbation of the acute inflammation.—This not infrequently arises from some indiscretion in diet, more especially the use of alcohol, from sexual excitement, or from unsuitable local treatment Such relapses may occur again and again, and not only greatly delay recovery, but are most potent factors in bringing about an extension to the posterior urethra, and in causing the disorder to become chronic.

ACUTE POSTERIOR URETHRITIS

About the beginning of the third week the inflammation in the anterior portion of the urethra reaches its acme, and, unless it extend farther along the urethra, will either entirely disappear or gradually pass into the chronic stage. Should it, however, extend to the posterior urethra, the prognosis is considerably more serious,

the risk of such complications as epididymitis, cystitis, prostatitis, and spermato-cystitis being very great.

Symptoms.—The extension of the inflammation to the posterior urethra may manifest itself by the sudden onset of painful symptoms, or it may occur so insidiously as hardly to attract the notice of the patient. The most frequent, and by far the *most distressing, symptom* is an excessive irritability of the prostatic mucous membrane, causing *a constant desire to micturate.* The intensity of this symptom is *proportionate to the degree of inflammation* In the acutest cases the desire to micturate scarcely ever abates, and is independent of the quantity of urine in the bladder.

Another common symptom is *hæmaturia.* The last few drops of urine and pus are stained with blood which has been pressed out of the inflamed mucous membrane of the membranous portion by the contraction of the compressor urethræ. As a rule, the bleeding is limited to a few drops of bright blood passed at the end of micturition, but at times the hæmorrhage is free This, unfortunately, often leads to an entirely erroneous diagnosis, and the unhappy patient is subjected to an instrumental examination of the bladder.

A third and usual *symptom is the occurrence of frequent seminal emissions*, due to the irritation of the caput gallinaginis. Its occurrence during the third or fourth week of an attack of acute gonorrhœa should cause the surgeon to suspect the presence of posterior urethritis. In addition to these three cardinal local symptoms, there is usually some constitutional disturbance, such as slight fever and a decided feeling of malaise

Diagnosis.—The easiest and, in most cases, the best way of proving the presence or absence of posterior urethritis is by means of the "two-glass test" of Sir Henry Thompson It is applied in the following manner: The patient, on rising in the morning, passes his urine into two urine-glasses, half emptying his bladder into the first, and then passing the remainder into the second glass. Should he be suffering from anterior urethritis, the urine in the first glass will appear turbid from the presence of pus, which the flow of urine has brought away; but the second portion of urine will be quite clear, for the urethra has been swept free of pus by the first portion passed. But if it be *a case of posterior urethritis, not only will the first portion of urine* be turbid, but the second also. It is obvious that this turbidity of the second portion can only be due to a turbidity of the urine within the bladder; *as the first portion of urine passed removes all the pus* from the urethra, if the urine within the bladder be clear the second portion must be clear also. The pus in the anterior urethra is prevented from passing backwards by *the strong compressor urethræ* muscle, but it is free to pass forwards, and is, indeed, aided by gravity.

But it is different with the pus found in the posterior urethra. Here the compressor muscle prevents it from passing forwards, it is free, however, to pass backwards into the bladder, where it mixes with the urine collected there. In this case both portions of the urine first passed in the morning are turbid, the first being as a rule the more turbid. But if the urine be tested in this way during the day, when it has not been retained for so long a period as during the night, it frequently happens that the second portion of urine is quite, or almost, clear.

This variation in the turbidity of the second portion of urine with the time of day is one of the chief diagnostic signs of posterior urethritis, and distinguishes it from cystitis, in which the turbidity of the urine is constant, and the second portion thicker than the first. Hence the importance of the rule, when testing for the presence of posterior urethritis, to examine the urine first passed on rising.

TWO-GLASS TEST

Acute anterior urethritis	*Acute posterior urethritis*	*Cystitis*
First portion cloudy Second portion clear.	First portion cloudy Second portion cloudy, though less so than the first portion.	First portion cloudy. Second portion always cloudy, generally more so than the first portion.

The **bacteriological diagnosis of gonorrhœa** is often of great value, especially in medico-legal cases and, as we shall see later, in forming a decision as to the definite cure of the chronic condition. In the acute stages, microscopic examination of a stained smear of the pus will usually definitely establish the presence or absence of the gonococcus; but it is to be remembered that the gonococci are not evenly distributed throughout the pus; therefore, several films should be prepared, and no antiseptic injection should have been made for some hours prior to the examination. Should no gonococci be found on the first examination, the search should be repeated on the following day, when, if they are still absent, it may be safely concluded that the case is not one of gonorrhœa. This, however, applies only to acute urethritis. In the chronic condition the gonococci are met with in spare numbers, and may be entirely absent from the secretion for days together. Moreover, their appearance is by no means so characteristic as in the acute stage, for the cocci are no longer found within the body of the pus cells, but free, or adhering to the surface of epithelial cells Hence their detection may require considerable bacteriological experience.

Morbid changes in the urethral secretion and mucous membrane.—It may be remarked that the nature and amount of a urethral secretion are generally better appreciated by an examination of the urine than by inspecting the secretion as it exudes from the meatus. This especially applies to the chronic condition of the disease; indeed, as we shall see later, it often happens that the only sign of a chronic urethritis is the appearance of the urine. Moreover, by the means suggested we are enabled to ascertain whether it be a case of gonorrhœa or not, without the patient being asked a single question or being aware of our suspicion The importance of this when dealing with women, or with men of a sensitive nature, will be readily appreciated. In the earliest stage of the disease, if the urine (and preferably the morning urine, for reasons which have been explained) be passed into a conical urine-glass, it will be noticed that floating in the clear fluid there are a few gelatinous thread-like bodies, which, if examined under the microscope, are seen to be composed of pus and epithelial cells held together by mucin. They are formed by the urinary stream detaching and rolling up the thin tenacious secretion produced by the inflamed mucous membrane. These filaments are known as "urethral threads."

As the disease advances, the urine will no longer appear clear, *but cloudy from the presence of mucus. The cloudiness then gives* place to a milky turbidity due to the increasing number of pus cells present. If the urine be allowed to stand a few minutes the pus *cells will sink to the bottom of the glass, forming a thick creamy sediment*, over which will be seen a light cloudy deposit of mucus In the further progress of the disease the layer of pus increases in amount, while the mucus diminishes. When the disease has reached its acme, little but pus is seen. As it abates, all these conditions are reproduced in an inverse order First the pus layer gradually diminishes in quantity, the mucus proportionately increasing; the mucus then disappears, and in the clear urine the urethral threads are seen floating; finally these disappear, and the disease is at an end

Much useful information may be obtained from a careful microscopical examination of the secretion, apart from the question of the presence or absence of the gonococcus. If the secretion be examined in the earliest stages of the disease, it will be noticed that the principal cells present, in addition to leucocytes, are large squamous epithelial cells; gonococci are numerous, either free or sometimes in the cells (Fig. 200). As the inflammation increases in severity, the leucocytes and gonococci become more and more numerous, the epithelial cells being less frequently seen. The pus cells then become crowded with the cocci. When the acme of the disease is passed and the pus changes to a muco-purulent secretion, it will be found

that the epithelial cells reappear, again mingled with the leucocytes The gonococci are still present, both free and in the pus cells, though in smaller numbers; but they are not seen within the epithelial cells, though often covering their surface.

In the latest stages of the disease both leucocytes and gonococci are met with but sparingly, the urethral threads showing the presence of transitional epithelial cells with few pus cells and cocci.

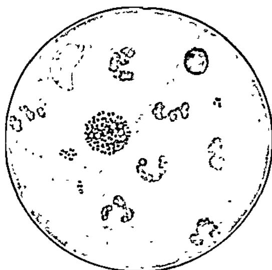


Fig. 200.—Acute gonorrhœal pus, showing gonococci and pus cells with irregular nuclei. × 1,000.

Treatment of acute urethritis.—The treatment of gonorrhœa may be conveniently discussed under three heads 1, Diet and hygiene; 2, internal remedies, 3, local applications

1. **Dietetic and hygienic measures.**—The importance of this part of the treatment is so fully recognized that it is unnecessary to dwell upon it at any length. Experience has abundantly proved the necessity for so regulating the patient's habits as to obtain the greatest amount of rest for the parts concerned, and the avoidance of frequent changes in the local blood supply. Everything which is likely to increase, even temporarily, the hyperæmia of the urethra is to be, as far as possible, avoided. It is with this object in view that the patient is placed on a light and easily digested diet, and forbidden to take alcohol in any form, or to indulge in violent exercises, such as riding, cycling, etc He must be also warned that the slightest sexual excitement is in the highest degree injurious, and is a frequent cause of retarded recovery; and energetic measures must be taken, if necessary, to

combat the tendency to protracted erections and nocturnal seminal emissions.

When it is impossible for the patient to remain in bed, the genitals should be supported by a well-fitting suspensory bandage, care being taken that this does not press unduly upon the penis or perineum. In no case should the selection of the bandage be left to the patient; the surgeon should do this himself, at the same time seeing that it is properly applied Some arrangement should be contrived for the absorption of the free purulent urethral discharge. It is not a good plan to insert cotton-wool under the prepuce, as is so frequently advised, for this is apt to hinder the free escape of the pus. A better method is to place the penis in a little absorbent-wool bag, such as is supplied by Hartmann's Wood-Wool Company. Finally, it is the duty of the surgeon to point out to the patient the highly contagious character of the disease, and the necessity for the most scrupulous care and cleanliness, lest infection be conveyed to others or the patient inoculate himself in other parts of the body, such as the conjunctiva or the rectum.

2 **Internal remedies.**—Although numerous drugs have been advocated from time to time as of use in the treatment of this disease, remarkably few have stood the test of time. Almost the only remedies which have proved themselves of any value are certain of the balsams, of which sandal-wood oil is the best. Copaiva, which is also largely used, possesses no advantages, and is decidedly more irritating to the stomach and kidneys. Although undoubtedly of some value in subduing the pain, these balsams do not cure the disease, and are accordingly to be used merely as adjuncts to the local treatment. They should be given only in the earliest stage of the disorder, and are of special value in those florid cases in which all local treatment is contra-indicated by the presence of pain and irritation. When taken by the mouth they are excreted more or less unchanged in the urine, and act as local sedatives and antiseptics to the inflamed mucous membrane. As a rule, they are beneficial and well tolerated; but they may entirely fail to cause any improvement, or may give rise to serious disturbance In either case a change of drug is indicated.

The most common ill-effects induced by sandal-wood oil and other balsams are nausea, dyspepsia and heartburn, and other evidence of gastric disturbance, cutaneous rashes, and irritation of the kidneys.

Vaccine treatment.—During recent years attempts have been made favourably to influence gonorrhœal inflammations by inoculating patients, either subcutaneously or intravenously, with some form of gonococcal vaccine or serum. Although a great deal of work has been done on this subject, opinions are still sharply divided as to the value of vaccine treatment; those with the greatest experience are the most reluctant to speak dogmatically. It is when the disease has given

rise to sharply circumscribed and more or less encapsuled inflammatory foci, as in prostatitis, salpingitis, and arthritis, that vaccine treatment is most likely to prove successful. Again, it is frequently employed in severe intractable metastatic inflammation which is inaccessible to local treatment, as in endocarditis, iritis, etc. This method of treatment is discussed at p. 127.

At first it was generally believed that, in order to obtain the best results, it was desirable that the vaccine should be prepared from a pure autogenous culture of the specific organism. More recently it has been shown that equally good results can be obtained from stock vaccines; even from the vaccines of other organisms, such as typhoid.

3. Local applications.—Local remedies have always played a large part in the treatment of urethritis, more especially since the microbic origin of the disease was determined; and there can be no question that the application of remedies directly to the affected part is both rational and highly successful; for though by means of dietetic and hygienic measures and the administration of balsams the disease can be greatly modified, these measures alone are rarely sufficient to bring about a complete cure.

If, from the mass of suggested remedies, we select those which have proved themselves to be of value, we shall find the list to be surprisingly small. Chief and foremost must be mentioned the old remedy, nitrate of silver, which is one of the most trustworthy of local applications. Unfortunately it is very irritating, even in dilute solutions; besides which it is readily decomposed by the chlorides present in the pus. Recently a number of combinations of this salt with various albuminous bodies have been placed on the market, several of which have proved to be valuable. The great advantage of these combinations is that they cause little or no pain or irritation when injected, and are not decomposed by the pus. Moreover, as they do not produce a coagulation of the albumin, they seem able to penetrate somewhat deeper into the tissues than pure nitrate of silver. The earliest of these preparations, argentamin and argonin, proved to be unstable, but the more recent compounds, protargol, hegonon, and albargin, are free from this defect.

Next in order of value to nitrate of silver and its compounds are solutions of permanganate of potash, sulphate of thallin, oxycyanide of mercury, sulphate of zinc, and sulphate of copper.

Such are, in general, the lines on which the treatment of acute gonorrhœa is based. It will now be convenient to consider the details of the treatment under two heads, viz.: (1) when the disease affects the anterior urethra only, and (2) when it affects the posterior urethra.

Treatment of acute anterior urethritis.—Although it is unusual for a hospital patient to apply for treatment until the discharge

is copious and the disease fairly advanced, it not infrequently happens that the more intelligent private patient seeks medical aid at the first sign of the disorder. In such a case the surgeon may feel tempted to try to cut short the malady by the application of some strong antiseptic remedy, but it must be remembered that the gonococci, within even a few hours of the inoculation, penetrate between the epithelial cells to the deeper parts of the urethral mucous membrane, in which situation they are effectually protected from the strongest antiseptics that can be applied. Moreover, the use of these strong antiseptics induces a violent inflammatory reaction, which is likely to aggravate the disorder to a great extent. For these reasons the use of powerful remedies, when the first symptoms of the disease are already present, has been abandoned

The abortive treatment is likely to prove successful in those rare instances only in which the patient seeks medical advice *immediately* after exposure to infection As the gonococci are then probably merely lying on the surface of stratified epithelium lining the fossa navicularis, the introduction of a relatively strong antiseptic fluid at this period may reasonably be expected to destroy the specific virus, and so prevent the development of the disease In the last few years this prophylactic treatment has received a good deal of attention, and during the War a considerable number of the men underwent some form of preventive treatment. In some countries prophylaxis was often made compulsory for all men on leave, or facilities were provided for disinfection of the genitals by the men themselves both before and after exposure to any risk. Naturally, the former method allowed of a far more thorough disinfection, and, where the treatment was adopted *within a few hours of exposure to* the infection, strikingly good results were obtained Provided this interval was short, the choice of disinfectant and the method of application seemed of little importance

The venereal statistics of the navy and of those camps where all night "passes" were forbidden—permission to leave the camp being restricted to a few hours—showed a marked superiority to the *statistics of camps where leave of absence was granted* for a period of twenty-four hours or more.

Of the many agents that have been employed for the purpose of disinfection, nitrate of silver is the most efficacious; a few drops of, say, a 1-per-cent. solution are introduced into the meatus before and after exposure. As we have seen, the nitrate is both irritating and easily decomposed; and this is true also of protargol and the other albu*minous compounds of this salt.* Hence, if the disinfection is to be left in the hands of the patient, some less irritating and more stable agent should be chosen Probably the best of those suggested is a 30-per-cent.

calomel cream, made with lanoline and soft paraffin. A small quantity of the cream is squeezed into the urethra and then the whole of the genitals, glans, prepuce, etc., freely anointed with the calomel ointment. If this be done in time, a considerable degree of protection from both gonorrhœa and syphilis is provided, though perfect immunity is certainly not achieved.

Although, as a rule, we may with advantage at once apply local remedies in the acute stage of the disorder, there are two conditions which contra-indicate this treatment. The first of these is an exceptionally acute inflammation, as evidenced by much œdema of the penis and prepuce, excessive chordee, and blood-stained secretion The other is the presence of a complication such as epididymitis. In either of these cases all local applications must be postponed until the more acute symptoms have subsided.

I usually begin the treatment by ordering the injection of ¼-per-cent. protargol solution[1] four or five times a day, the fluid to be retained in the urethra five minutes. The effect of this treatment is generally very marked: the purulent discharge rapidly diminishes, and the pain and priapism disappear. When these effects are secured, the strength, duration, and frequency of the injections may be gradually increased. At the end of the third day the strength of the fluid may be raised to ½-per-cent. solution, at the end of the week to ¾-per-cent., and on the tenth day to 1-per-cent. At the same time the injections are given more frequently—four, five, or six times a day—and the fluid retained for five minutes or longer. This is all contingent upon the injections being well borne, causing neither smarting nor discomfort, and upon the inflammatory symptoms declining

Under the above treatment the inflammatory symptoms usually abate rapidly, the priapism and pain on micturition cease, and the secretion diminishes greatly in quantity, and becomes less purulent and more mucoid in character; the pus cells are less numerous, and epithelial cells reappear; the gonococci are no longer seen in large numbers, and almost entirely disappear. When this change has taken place, usually in the second week, the injection fluid should be altered to one having more astringent properties Twice a day, morning and mid-day, permanganate of potash (1 : 10,000) may be used, and in the evening nitrate of silver (1 : 10,000) The strength of the latter may be cautiously increased from time to time, for the urethra quickly becomes tolerant of these antiseptics, so that a solution which at first causes smarting and discomfort, in a day or two is hardly felt. For the

[1] The protargol solutions should be freshly made with cold distilled water, as heat decomposes the compound. If the urethra is very sensitive, antipyrin or nitrate of novocain to the extent of 3 per cent. may be added with advantage to the protargol solution.

same reason it is well occasionally to vary the nature of the injection. It must be understood that the strength of the solutions mentioned above represents but an average useful strength. The more acute the inflammation, the weaker must be the injection. The effect of the astringent treatment is soon noticed; the discharge rapidly diminishes, until it disappears.

At this stage the patient, being free from pain and not seeing any discharge, will almost invariably believe himself to be cured, and, unless convinced of his error by his medical attendant, will withdraw himself from all further treatment. Should he do so and return to his former mode of living, in all probability the discharge will reappear; *for the gonococci, not being completely eliminated, will, in favourable circumstances, rekindle the inflammation.* In the normal course of the disease a cure is rarely obtained under five or six weeks, and this period will be prolonged if exacerbations or complications take place.

Should the disease still persist at the end of the sixth or eighth week, as evidenced by the presence of mucus and "threads" in the urine, it must be regarded as having passed into the subacute or chronic stage, and as requiring treatment appropriate to that condition. (*See* p. 863.)

Treatment of acute posterior urethritis.—As the extension of the inflammation to the posterior part of the urethra does not usually take place until about the end of the third week, the case is generally under treatment when this complication appears. If the spread of the inflammation gives rise to very acute symptoms—hæmaturia, frequent micturition, or seminal emissions—all injections should be stopped until these symptoms have died down. As in anterior urethritis under similar circumstances, the treatment must be purely constitutional, all local interference tending to aggravate the inflammation.

1. *Constitutional treatment.*—The constitutional treatment is the same as that for anterior urethritis, except that salicylate of soda is generally more useful than the balsams. This drug, though of comparatively little value in inflammation of the anterior urethra, has a very beneficial effect in posterior urethritis. Under its action
the urine rapidly clears and the acute distressing sy
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Apart from the administration of salicylate of soda, the treatment must also be directed to combating the three prominent symptoms of acute posterior urethritis—vesical tenesmus, hæmorrhage, and seminal emissions. The first may be mitigated by sedatives and the use of hot sitz-baths As a rule, the slight hæmorrhage which accompanies the vesical tenesmus is best treated by the sedatives mentioned above. When of a severe character and unaccompanied by vesical tenesmus, it may be restrained by the instillation of novocain (2 per cent.) and adrenalin (1 : 1,000). The tendency to frequent seminal emissions, which is so common a feature of this disease, must be energetically combated, for the intense hyperæmia they cause is in the highest degree injurious. For this purpose, bromide of potassium, monobromide of camphor, and heroin are generally the most useful drugs

The importance of rest in the treatment of acute gonorrhœa has already been noticed, but it must be emphasized in connexion with acute posterior urethritis

2. *Local treatment.*—The principles of treatment for acute posterior urethritis are the same as those laid down for acute anterior urethritis, namely, to withhold all local applications during the most acute stage of the disease When this has passed, and as the inflammation subsides, the bland antiseptics may be used, and gradually changed to more astringent ones. The application of these remedies requires certain modifications of the method advocated in the preceding section. When, and not until, the tenesmus and other painful symptoms have quite disappeared under the constitutional treatment, the local applications may be begun by ordering the patient a dilute solution of protargol ($\frac{1}{4}$ to $\frac{1}{2}$ per cent.) or sulphate of thallin (1 per cent.). The solution may be injected three or four times a day, in the manner described when speaking of acute anterior urethritis As these fluids are non-irritating, they do not usually produce a powerful contraction of the compressor urethræ muscle, and so pass gradually into the posterior urethra. The injection should be retained in the urethra for fifteen minutes, so that the primary contraction of the compressor urethræ may relax and allow the fluid to pass backwards. The patient should be instructed to aid the passage of the fluid by relaxing as far as possible—that is to say, he should try to micturate while the injection is being made. The beneficial effect of the injections is generally quickly seen. Within a few days the purulent secretion diminishes and becomes more mucoid in character. When this takes place and all painful symptoms are absent, the astringent remedies may be applied. But it is useless to order their injection with the ordinary gonorrhœal syringe; the fluid will not pass the compressor urethræ, which is thrown into strong spasm by the irritating solution. This difficulty may be overcome by either of two methods—we may gradually increase

the pressure of the fluid injected at the meatus until it is sufficient to overcome the spasm of the compressor urethræ (Janet's irrigation), or we may inject the fluid by some suitable instrument, such as a catheter.

Janet's irrigation is carried out by means of an irrigator which contains a pint or more of fluid, fitted with a couple of yards of tubing and a conical glass cannula. Fig. 201 shows Valentine's instrument for the purpose. The temperature of the irrigation fluid should in all cases be from 38° to 40° C. The patient having first half-emptied the bladder, so as to clear the urethra of pus, the end of the glass cannula is inserted into the meatus and the irrigator raised a foot or two. The pressure of the fluid suffices to distend the anterior urethra, but not to overcome the compressor muscle. The *cannula is then removed*, and the fluid allowed to escape from the urethra. After this has been repeated two or three times with a view to the thorough washing out of the anterior urethra, the cannula is reinserted, and the irrigator raised until the pressure of the fluid is sufficient to overcome the compressor muscle; the *lotion then enters* the posterior urethra and passes into the bladder. As a rule, the irrigator must be raised about 1½ yards before the resistance of the compressor muscle is overcome. The irrigation is best done with the patient lying on his back with the legs apart. As the irrigator is being raised, the patient should be instructed to relax the urethral muscles by trying to micturate. It is by no means always easy to inject into the posterior urethra in this way, the dis-

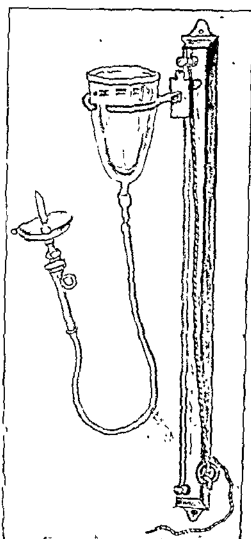


Fig. 201.—Valentine's urethral irrigator.

tension of the urethra sometimes causing severe pain. When this is the case it is well to give a small preliminary injection of a weak novocain solution (1 per cent) a few minutes before irrigating.

The principal advantage derived from this method is that the pressure of the fluid, by stretching the urethral mucous membrane and obliterating its folds, ensures the lotion coming into contact with its entire surface.

Abundant experience has demonstrated that the fear of infecting the bladder by these methods of irrigation is groundless. The fluid injected into the bladder does not require to be removed by the surgeon; it is passed naturally at the close of the procedure

It is best to select at first very weak solutions of mild remedies, such as protargol (¼ to ½ per cent) or sulphate of thallin (1 per cent.), and after a few days to pass on to stronger and more astringent solutions, such as permanganate of potash (1 : 10,000 to 1 : 2,000) or nitrate of silver (1 : 10,000 to 1 . 500) As a rule, the nitrate-of-silver solutions are the most efficacious

The irrigation is performed by the surgeon every two or three days, the patient continuing his injections with the small syringe two or three times each day.

CHRONIC URETHRITIS

Pathology.—There is naturally no sharp line to be drawn between the morbid processes observable in the acute and the chronic forms of this disease, the one merging imperceptibly into the other. The inflammation subsides, and, losing the general, diffuse distribution of the acute stage, lingers only in more or less circumscribed areas. Here, in consequence of the prolonged irritation from the gonococci, there is induced a proliferation of the subepithelial tissue cells, forming the so-called small-celled infiltration. This proliferation of the connective-tissue cells is always a well marked feature in the chronic stage, but a certain degree of proliferation is present even in acute cases. The areas of "small-celled" infiltration are generally localized in small foci round or in the neighbourhood of the lacunæ and ducts of the mucous glands. They are often extremely vascular, and present a granular appearance

The epithelium beneath which they are developed may remain either unchanged or but slightly œdematous and loosened. Erosions or ulcerations are decidedly rare. After a time, spindle-shaped connective-tissue cells, and later definite fibres of connective tissue, are developed in the areas of infiltration. The soft character is lost, and the areas gradually become converted into dense fibrous or scar tissue At the same time the epithelium lying over the areas

also undergoes a metaplasia, gradually losing its cylindrical form and assuming a stratified squamous type.

As a rule, the inflammation does not extend beyond the subepithelial tissue, the deeper structures being unaffected. When, however, the periurethral tissues become involved, the subsequent cicatricial contraction causes a diminution in the calibre of the urethra, and so gives rise to the formation of a stricture.

Symptoms.—When the inflammation is limited to the mucous membrane, it causes but little inconvenience to the patient. There is usually a complete absence of pain on micturition, though sometimes a slight irritation is felt at the end of the penis. The most noticeable symptom is the well-known bead of purulent secretion which is found at the meatus on waking in the morning, and is aptly called the "bon-jour drop" The secretion is so slight that during the day, when the urethra is frequently irrigated by the stream of urine, the drop of pus may not be seen, though the lips of the meatus may stick together.

If the urethritis be fairly recent, the first portion of urine will be turbid from mucus, and will show the presence of urethral threads. If the process be of long standing and free from any exacerbation, the urine will be quite clear and free from mucus, but will show the threads floating in it. *Often the only sign of a chronic urethritis is the presence of a few urethral threads floating in the urine first passed in the morning*, the secretion in such cases being too slight and tenacious to appear at the meatus as the "bon-jour drop." Should the inflammation extend to the tissues beneath the mucous membrane, other and more serious symptoms are likely to develop; for, as the small-celled infiltration gradually undergoes cicatricial contraction, the lumen of the urethra is diminished, and the symptoms of a stricture are added to those described above.

Should the deeper structures of the posterior urethra become involved, distressing urinary, sexual, and general nervous symptoms will be evoked in consequence of the irritation of that highly sensitive organ the prostate.

Examination.—*Before treatment is begun the establishment* of an exact diagnosis is essential. We must know not only whether the urethra is inflamed or not, but also whether or not the gonococcus is still present. Are other micro-organisms present in the secretion, and if so, what is their nature? Where is the inflammation situated, in the anterior or the posterior urethra? Is the inflammation limited to the mucous membrane, or has it extended to the deeper structures? Is there any diminution of the calibre of the urethra? Has the inflammation spread to other organs, such as the bladder, prostate, seminal vesicles, etc.?

To answer these questions a full and systematic examination of the patient is necessary. The steps of the bacteriological examination and the method of determining whether the inflammation affects the anterior or the posterior urethra have been considered above, in connexion with the diagnosis of acute urethritis

The *simplest method* of ascertaining the character of the inflammation in chronic urethritis is to pass a large acorn-headed black-gum bougie down the whole length of the urethra (Fig. 202). If the head of the bougie passes over the inflamed area a twinge of pain is felt by the patient, which ceases as soon as the head has passed beyond the affected spot, but is again felt as the head passes over it when the bougie is being withdrawn. By noting these sensitive spots the seat and the extent of the inflammation may be determined. Moreover, the passage of a large acorn-headed bougie proves the absence of any decided stricture of the urethra; the determination of this fact is of the greatest importance.

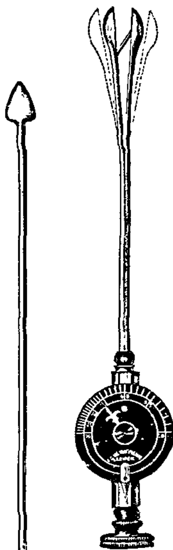


Fig. 202. Acorn-headed black-gum bougie.

Fig. 203. Weir's urethrometer.

A better method of ascertaining the degree of contraction is by the use of the urethrometer. This instrument, when introduced into the urethra, can be expanded at will, the degree of expansion being indicated by a pointer on a dial (Fig 203). The dilatability of the normal urethra in its various parts has been given on p. 839. Any inflammatory infiltration renders it less and less dilatable, according to the depth to which the infiltration has penetrated and its advancement towards fibrosis A very good idea of the extent and depth of the inflammation can be arrived at by carefully noting the amount of dilatation.

Lastly, the urethral mucous membrane should be examined by means of the endoscope, for by this means alone can we detect many of the minute changes in the inflammation of the mucous membrane, which would otherwise pass unnoticed, and the observation of which is, in many cases, essential to successful treatment. In its simplest

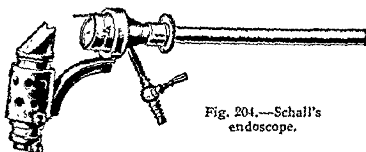


Fig. 204.—Schall's endoscope.

form the endoscope consists solely of a straight metal tube, having a funnel-shaped opening at one end; the tube being introduced into the urethra, the light is reflected down the funnel-end by means of a mirror. The illumination is so imperfect that the instrument in this form is of little value. To correct the defect several modifications have been devised, of which Schall's and Valentine's are to be preferred. In Schall's instrument (Fig. 204) the light from a small incandescent lamp is reflected by means of a prism down the urethral tube. In Valentine's (Fig. 205) the source of light is a minute incandescent lamp mounted on a rigid metal wire, which is passed down the tube, and so directly illuminates the portion of membrane under observation.

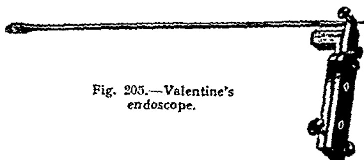
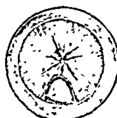


Fig. 205.—Valentine's endoscope.

In the normal condition, except during micturition, the walls of the urethra are in contact, lying in longitudinal folds. The passing of the urethroscope separates the walls; but as it is being withdrawn they fall together again, at a short distance from the end of the tube, in the form of a funnel, the folds radiating from a central point, which has much the appearance of a sphincter, and is called "the central figure" (Fig. 206).

In the normal condition of the prostatic urethra the mucous membrane is smooth and of a deep-red colour. As the tube is withdrawn the mucous membrane becomes paler, and a rounded prominence appears at the lower edge of the tube; this prominence represents the caput gallinaginis (Figs 207, 208). As the tube is still further with-


Fig. 206.


Fig. 207.

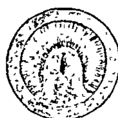
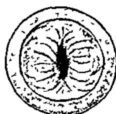

Fig. 208.

Fig. 206 —Membranous portion of normal urethra, as seen through the endoscope, showing small round central figure with numerous fine radiating folds.
Fig 207 —Normal prostatic urethra, showing the anterior portion of the caput gallinaginis
Fig 208 —Normal prostatic urethra, showing the caput gallinaginis.

drawn the caput disappears from view, and the membranous portion is inspected. This is generally paler in colour than the prostatic, and the central figure is more regular. In the bulbous part the folds of mucous membrane are larger, and the central figure appears as a vertical fissure (Fig. 209), and at times the openings of Cowper's glands can be seen in the floor. In the penile part the opening of the glands of Littré and Morgagni can be seen in the upper and lower


Fig. 209.

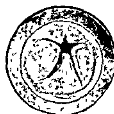

Fig. 210.

Fig 209 —Normal urethra in the middle of the bulbous portion. Central figure vertical
Fig. 210.—Appearance of chronically inflamed urethra, showing an old infiltration area in the penile portion Central figure gaping longitudinal folds less numerous and less marked than normally

walls of the urethra. In the glans the membrane has almost lost its red colour, and the round central figure has become triangular.

Appearance of the chronically inflamed urethra.—Two forms of inflammatory lesions can be seen by the endoscope in chronic urethritis. The first is that described, when speaking of the morbid anatomy of the condition, as consisting of localized small-celled infil-

tration of the subepithelial tissue, causing swelling and hyperæmia of the mucous membrane. This represents the "soft infiltration" of Oberländer, and is the early stage of the chronic gonorrhœal process. The second group of pathological changes forms what Oberländer calls the "hard infiltration." It includes all the inflammatory processes by which the small-celled soft infiltration gradually passes into firm fibroid scar tissue, which reaches its highest development in the formation of a stricture. The conversion of a soft-infiltration area into firm cicatricial tissue is a gradual process, all the phases of which can be observed by the urethroscope.

Soft small-celled infiltration.—In the soft small-celled infiltration in its most typical stage the mucous membrane is hyperæmic and redder than normally. Its epithelium is œdematous, dull, and loosened, so that it is readily detached, and may be altogether absent in places,

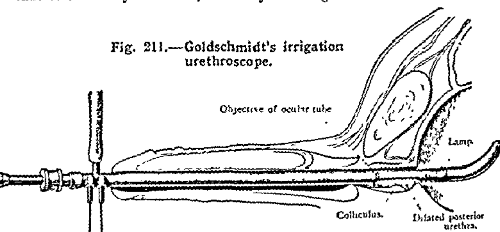


Fig. 211.—Goldschmidt's irrigation urethroscope.

leaving small erosions which bleed on being touched by a probe. In consequence of the swelling and œdema of the mucous membrane, the longitudinal folds, into which the urethra is normally thrown when the passage is not distended, are coarser and less numerous. Instead of seeing several fine folds radiating from the central figure, as normally, three or four thickened folds press forward into the lumen of the endoscopic tube. In the penile portion the openings of the crypts of Morgagni are seen to be reddened and swollen, whilst in the prostatic urethra the principal changes are grouped around the caput gallinaginis, which is swollen and hyperæmic, and projects into the tube, looking not unlike a ripe raspberry.

Hard infiltration.—*Pari passu* with the gradual cicatrization of the soft small-celled infiltration, the hyperæmia, turgescence, and elasticity of the affected mucous membrane diminish The red, angry-looking membrane becomes paler and paler as the infiltration hardens. The epithelium becomes thicker and less transparent; frequently it takes

on a curious stippled appearance, and may undergo so marked a proliferation as to give rise to a form of pachydermia. The longitudinal folds of the mucous membrane gradually disappear, becoming both less marked and less numerous (Fig 210)

The urethra as it appears during the process of healing. —The gradual healing of the inflammatory process under appropriate treatment can be readily observed by means of the endoscope. The mucous membrane covering the soft infiltration gradually loses its angry red colour, and regains its normal appearance. As the swelling of the membrane dies down, the longitudinal folds become finer and more numerous, and the lining epithelium regains its bright, transparent, glistening appearance. It is around the crypts and follicles of the urethra that the inflammation is seen to linger longest. Long after the rest of the urethra has regained its healthy appear-



Fig. 212.



Fig. 213.

Orifice of the normal bladder and colliculus seminalis as shown by Goldschmidt's urethroscope

ance a zone of inflammation may be seen to surround the openings of the large lacunæ and glands, from the mouths of which a mucopurulent secretion may occasionally be expressed

Goldschmidt's irrigation urethroscope.—A urethroscope constructed on an entirely new principle has been introduced by Goldschmidt of Berlin (Fig 211). It consists of a clever adaptation of the ocular arrangement of Nitze's cystoscope to the requirements of the urethroscope The urethra is examined whilst distended by a current of warm water, which runs from an irrigator into the bladder, and, by holding the walls of the canal apart, permits of an extensive view. The appearance of the urethra (Figs. 212, 213), as seen by this instrument, is strikingly different from that obtained by the ordinary urethroscope, for not only does the mucous membrane look pale and anæmic, but the form and character of the lumen appear quite different. This is especially evident in the posterior urethra, in the examination of which the great value of the instrument lies; indeed, the instrument is rarely used for the examination

of the anterior portion. One sees the colliculus seminalis and the openings of the prostatic and ejaculatory ducts with a clearness and vividness which is startling to those only accustomed to the imperfect and distorted view obtainable by the older form of instrument. Whilst watching the colliculus, not infrequently one may observe the ejaculation of the spermatic fluid from the ducts, provoked by the stimulation of the urethroscopic tube; or one may watch the expression of the secretion when the prostate is massaged On introducing the instrument a little farther, the orifice of the bladder can be seen and examined in a way which hitherto has been impossible either by the cystoscope or the urethroscope (Figs. 214, 215). Here, again, the instrument is a valuable aid to diagnosis in many obscure cases of vesical and prostatic trouble, quite apart from those arising from gonorrhœa Goldschmidt's urethroscope has been



Fig. 214.



Fig. 215.

Fig 214—A chronically inflamed colliculus seminalis which has developed several fine, villous-like growths.

Fig 215—An inflamed and swollen colliculus, with irregular foldings of the mucous membrane at the sides

modified in various ways by Wossidlo of Berlin, Buerger of New York, Luys of Paris, and others, especially with a view to the treatment of chronic inflammatory foci by local applications or cauterization.

Treatment.—All cases of chronic urethritis can be divided into two groups:—

1. The more recent, or subacute, where, in addition to the localized areas of cellular infiltration, there is a more or less general catarrhal inflammation of the mucous membrane.

2. The inveterate or circumscribed, in which there is no general catarrh, the whole trouble being confined to definite localized portions. This group may again be divided into (a) those that affect only the mucous membrane, and (b) those that affect the submucous tissue also. Each of these forms requires a different mode of treatment.

1. Treatment of subacute urethritis.—The first aim must be to subdue the general catarrhal condition of the mucous membrane, leaving the areas of cellular infiltration to be treated later Experience has shown that the best means of effecting this is the irrigation of the canal with mild astringent solutions. For this purpose the ordinary small urethral syringe is rarely suitable, for, as has been already explained, the anterior urethra is seldom affected alone in chronic gonorrhœa, the inflammation generally extending to the posterior portion; consequently the use of the small syringe for injection would probably leave a large portion of the inflammation untouched. This is one of the commonest errors in the treatment of gleet. It is essential for success that the irrigation fluid be brought into contact with the whole of the walls of the urethra This may be accomplished, as has been shown in the treatment of the acute stage of posterior urethritis, by gradually increasing the pressure of the fluid injected at the meatus by means of the irrigator (Fig. 201) or the large syringe (Fig 216) until

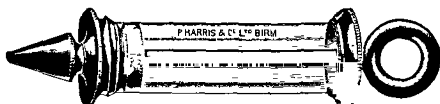


Fig. 216.—Large syringe for irrigating the urethra.

it is sufficient to overcome the spasm of the compressor urethræ. Another method is to inject the fluid by means of a soft rubber catheter passed into the posterior urethra (Diday's irrigation). It is well to select that method which causes the patient the least discomfort. As a general rule, it will be found that Janet's method of irrigation is the best; but in every case the irrigation must be given by the surgeon. To allow a patient to treat himself is to invite disaster. The only injection it is safe to leave in his hands is that given by the small urethral syringe.

The injection fluid—Experience has shown that the organic combinations of silver, as protargol and argonin, have not the same value in the chronic that they have in the acute forms Consequently, as a rule, the simple, freely diluted nitrate of silver (1 : 20,000 to 1 : 5,000) is to be preferred. Other solutions valuable at this stage of the disease are permanganate of potash (1 : 10,000 to 1 : 2,000) and sulphate of zinc (1 : 2,000 to 1 : 1,000)

2 Treatment of inveterate or circumscribed urethritis.—(a) In the superficial form of this variety of urethritis, where the mucous membrane only is involved and there is neither a narrowing

to 18 or 20. But even with these large bougies the urethra cannot always be thoroughly dilated, for the largest bougie that the fully stretched meatus will admit is too small to distend fully both the bulbous and the prostatic portion.

An instrument is sometimes needed which, like the urethrometer, can be passed through the narrow part, and then expanded at will. Such an instrument is provided in the urethral dilators[1] of Oberländer (Fig. 220), Kollmann (Figs. 221, 222), and others. The dilator, well lubricated with glycerine and tragacanth, is passed down to the affected portion of the urethra, and then by means of the screw slowly expanded. The degree of expansion is indicated on a dial. The dilatation must be very gradual, not more than 1 mm. at a sitting, and must be stopped immediately it occasions pain; it should not give rise to bleeding. After an interval of seven or eight days, when all reaction has died down, the dilatation may be carried to a further degree. After each dilatation the urethra must be irrigated with a dilute antiseptic, such as nitrate of silver lotion (1 : 10,000). In the interval, astringent irrigations, Janet's or Diday's, should be used. As long as the secretion contains numerous gonococci, instrumental interference of any kind is best withheld, but the presence of a few of the micro-organisms is not in itself a contra-indication to treatment by dilatation.

It is advisable in all cases to begin the dilatation treatment with bougies, as they cause far less irritation to the urethra than the dilators If the meatus is moderately wide the passage can generally be dilated without discomfort up to No. 26 to 27, and often to No. 30 (French scale). In the majority of cases it is unnecessary to use the dilators at all, as the degree of expansion obtained by the large bougies is sufficient to bring about a cure.

Throughout the whole treatment it is most important that the progress of the case be controlled by frequent microscopic examinations of the secretion and the use of the urethroscope.

GONORRHŒA IN WOMEN

The recognition of the gravity of this disease in women has been tardy; indeed, at one time it was held that the infection was restricted to the vulva and vagina and that it showed no tendency to spread or to become chronic. This view, now known to be diametrically opposed to the truth, was probably due to the ease with which the condition can be overlooked in the female. Women, less versed and less interested in genito-urinary diseases than men, and accustomed to

[1] These urethral dilators are made in various forms. Figs. 220, 221 represent instruments designed to dilate the anterior urethra, Fig 222 the posterior, and Fig. 223 both anterior and posterior.

periodic pain and discomfort in the pelvic organs, are apt to attribute their symptoms to other causes, or even to imagine them inseparable from the conditions of early married life. Moreover, in any save the acute stages of the disease, both the physical and the bacteriological methods of diagnosis are much more difficult than in men.

In its etiology, period of incubation, pathology, and general course the disease does not differ from that in the male. The site of the inoculation varies according to age: in young children it generally takes place at the vulva; in adults the urethra and the endometrium of the cervical canal of the uterus are usually first affected. But in the great majority of acute cases the inflammation, wherever it starts, soon spreads to all these regions and, in a considerable number of cases, also to the uterus, tubes, and pelvic peritoneum.

Diagnosis.—The acute stage rarely offers any difficulty. After the usual incubation period an acute catarrhal inflammation develops, and rapidly spreads over the sexual organs. The nymphæ and clitoris are red and swollen and often the seat of small superficial erosions. The orifice of the urethra is congested and pouting, and, if a finger be placed in the vagina, the urethra will be felt as a firm, tender cord, from which a bead of pus may be squeezed. The demonstration of an acute urethritis is in itself almost pathognomonic of gonorrhœa; should the pus from it show the presence of the gonococcus, the diagnosis is, of course, established.

The diagnosis in the subacute and chronic stages is much less easy, and requires considerable experience on the part of the surgeon to justify a definite statement in a given case. The detection of the specific organism is difficult, for the normal secretion of these parts always shows the presence of numerous micro-organisms; amongst them many diplococci, closely resembling the gonococcus.

When examining for suspected chronic gonorrhœa, the following points should be sought for:

1. Signs of inflammation of Bartholin's gland The duct of this gland opens just in front of the hymen, and, when inflamed, is frequently surrounded by a dark purple-red zone (the macula gonorrhœica of Sänger), and pressure on the gland expresses a purulent or mucopurulent secretion

2. Condylomata or warts about the vulva.

3. Signs of a chronic urethritis As this condition in women gives rise to no subjective symptoms, and as the two-urine-glass test is not applicable, the condition can only be recognized by careful examination, including the use of the urethroscope

If the meatus be carefully cleaned and pressure made on the urethra from behind forwards, a bead of muco-pus can generally be expressed, which should be selected for bacteriological examination.

4. The presence of a purulent or muco-purulent discharge from the cervix uteri.

5. Evidence of inflammation of the uterus and adnexa.

6. A history of ophthalmia neonatorum in one or more children.

Symptoms.—After a short period of incubation, of from two to six days, symptoms of a slight inflammation of the vulva and urethra develop. At first merely a sense of local heat and discomfort is felt, which soon increases to one of considerable irritation, accompanied by a smarting and burning pain on micturition. There are swelling and œdema of the external genitals and exudation of a profuse purulent discharge between the labia. The symptoms are at their height about a week from the time of onset and, under favourable conditions, begin to decline about the third week. The inflammation rarely remains localized to the site of inoculation, but spreads until it affects the greater part of the sexual organs, so that in many cases the symptoms of acute endometritis, salpingitis, and pelvic peritonitis are superadded to those already mentioned

There is still much uncertainty as to the frequency with which the uterus and adnexa are involved, but recent investigations lend support to the view that these organs seldom wholly escape.

Prognosis.—The prognosis of gonorrhœa in women is always far graver than in men. Although the symptoms evoked are often so slight as barely to call the patient's attention to the fact that anything is wrong, yet *the outlook, both as regards the general health and the duration of the disease, is much more serious than is generally believed.* The death-rate due to the disease in women is quite unknown. The official statistics are untrustworthy, for it is probable that in the majority of fatal cases the complaint is either unsuspected or for social reasons not stated. Apart from these fatal cases, there are many where, as a consequence of some complication, the general health of the patient is severely affected. There are few pictures sadder than that which too frequently meets the surgeon's eye in the rapid transformation of a bright, healthy girl into a peevish, chronic invalid in consequence of a gonorrhœal infection acquired early in married life.

Treatment.—The treatment of this disease in women is surrounded by many difficulties, and is, as a rule, very imperfectly carried out. In the main it proceeds on lines similar to those laid down in connexion with the male.

In the acute stage, emphasis should be laid on the necessity for complete rest and a light diet, and the avoidance of alcohol and other irritants Internally, the balsams and copious drinks of bland fluids may be prescribed, with a view to diminishing the urethral irritation.

Locally, the parts must be kept clean and provision made for the absorption of the copious discharge. Hot sitz-baths and the application

of fomentations may be employed for the relief of the pain. As soon as the patient can tolerate it, the vulva and vagina should be freely irrigated two or three times a day with hot solutions of permanganate of potash (1 : 5,000 to 1 : 2,000) or protargol (1 : 1,000); as the inflammation subsides, the strength of these lotions should be increased, or be superseded by 1 : 1,000 to 1 : 250 of nitrate of silver.

In the subacute and chronic stages, in addition to these irrigations, more powerful solutions may be occasionally applied, say by a cotton swab, directly to the cervical canal, the vagina, and the urethra, or rod-shaped pessaries formed from cacao butter and impregnated with protargol (2–5 per cent.), iodine (1 per cent.) or nitrate of silver (1 per cent.) may be introduced into the cervical canal and the urethra.

It is useless at this stage to attempt to influence the disease by the administration of balsams and such remedies. The only constitutional treatment which holds out any promise of success is some form of vaccine-therapy.

Should Bartholin's gland inflame and suppurate, it should be freely incised and packed with gauze.

For the treatment of gonorrhœal inflammation of the uterus and tubes the reader is referred to the article on the Female Genital Tract, in Vol. III.

SOFT CHANCRE (CHANCROID, ULCUS MOLLE)

Soft chancre is a highly contagious venereal disease, characterized by the occurrence of one or, more frequently, several shallow ulcers about the genitals. The disease is due to inoculation with a specific micro-organism (Ducrey's bacillus), and has no connexion with syphilis, with which until comparatively recently it was confounded. It is to be noted, however, that the virus of syphilis and that of soft chancre may be, and indeed often are, inoculated at the same time in the same place. In such cases the soft sore develops first, and about a month later symptoms of syphilis supervene.

The incubation period of the disease is short, so that within a few hours after infection a hyperæmic spot may be seen at the site of the inoculation, and in twenty-four to forty-eight hours a pustule may have developed. A little later the pustule bursts, leaving a shallow ulcer. When fully developed, the appearance of the ulcer is characteristic. It is generally round, and has sharp punched-out edges which may be slightly undermined. The floor of the ulcer is usually uneven and ragged, and covered at first with a greyish-white slough, and later with more or less healthy granulations; the base is invariably soft. The secretion is intensely infective, and auto-inoculation frequently takes place. As a rule the ulcer remains small, about the

size of a threepenny-bit; occasionally, on the skin of the thigh or abdomen, it attains a very large size.

Duration.—From three to six weeks is about the average duration of an uncomplicated soft sore.

Localization.—In the male the chief seat of the ulcer is the prepuce or glans penis; more rarely it is met with in the urethra, where it is likely to be mistaken for gonorrhœa. In women it is most frequently seen about the fossa navicularis, the clitoris, and the meatus urinarius; also about the labia majora and the anus. On rare occasions the ulcers have been noted on the finger, lip, conjunctiva, etc.

Complications.—Apart from such minor complications as phimosis or paraphimosis as a result of the inflammatory œdema of the prepuce, there are two more severe troubles which deserve mention. One of these—acute inflammation of the inguinal lymphatic glands—is of very common occurrence In men about one-third to one-half of all cases of soft sore develop an acute adenitis. In women it is less common. It may arise at almost any period of the disease, but is most frequently seen in the second week. One or more of the glands in the groin become enlarged and tender, the temperature is elevated, and in the course of a few days the gland breaks down and forms an abscess, which, if unopened, undermines the skin and is evacuated spontaneously, leaving a rugged and indelible scar.

The second complication, phagedæna and gangrene, is happily decidedly rare, for it is always serious and difficult to treat. It is met with most frequently in neglected, filthy, and debilitated subjects. The ulceration assumes an unhealthy sloughy appearance and steadily extends. causing grave destruction of tissue. Usually it spreads superficially, at times deeply. Its course may be rapid, but commonly it is very slow, often resisting all treatment for weeks or months.

Gangrene may arise as a complication of soft sore in a variety of ways. Perhaps most commonly it is seen as a consequence of the circulatory disturbance occasioned by a tight phimosis or paraphimosis. At other times it is to be traced to a general constitutional disease, such as diabetes. It is most serious if associated with phagedæna, when grave and extensive destruction of the tissues may take place.

Prognosis.—The prognosis should be guarded; for not only is the condition at times troublesome to cure, but the possibility of syphilis being also engrafted must be borne in mind.

Treatment.—In uncomplicated cases the treatment is purely local. The ulcerated surface is cauterized with fuming nitric acid, or other strong caustic liquid, and then powdered with iodoform, aristol, dermatol, or other antiseptic preparation, and kept as clean and as free from irritation as possible.

At the first sign of an inguinal adenitis, rest in bed should be enforced, and an ice-bag or a light elastic dressing applied to the groin. Should suppuration threaten, an attempt may be made to abort the inflammation by the injection of an antiseptic into the substance of the gland. Or the formation of pus may be hastened by the application of warmth and then, as soon as fluctuation can be detected, the pus evacuated by a small incision, and half a drachm to a drachm of a 1-per-cent. solution of nitrate of silver injected. The injection must be repeated daily for two or three days, and the small incision kept open by a minute tube or iodoform gauze drain and the application of a wet boric-acid dressing.

In this way it is often possible to effect a cure of the adenitis with a minimum of disturbance and loss of time. Failing that, the abscess must be opened and treated on general surgical lines A vertical incision remains patent more readily than an oblique inguinal one.

By far the best treatment for a phagedænic condition is the use of continuous warm baths and the cautious application of the Paquelin cautery. The debilitated constitution must be supported by nutritious liquid food. When gangrene is threatened, every effort must be made to overcome the hindrance to the circulation. A tight phimosis or paraphimosis must be operated upon and any necrotic edges removed.

COMPLICATIONS OF GONORRHŒA

BALANITIS

Balanitis is the term applied to an inflammation of the mucous membrane covering the glans penis and lining the prepuce. It may be caused by almost any source of irritation to the end of the penis, but much the commonest is the retention and decomposition of the smegma secretion behind a tight foreskin, either alone or in association with other causes of irritation, such as a soft sore, a true chancre, epithelioma, herpes, or eczema. In gonorrhœa its occurrence is to be attributed to the additional irritation produced by the urethral discharge retained and decomposing behind a long prepuce; the gonococcus seldom directly causes the balanitis.

Symptoms.—The inflammation of the glans produces an itching and soreness of the end of the penis, which becomes red, swollen, and œdematous, whilst from beneath the foreskin a free and intensely fetid discharge exudes. If the prepuce be drawn back, the mucous membrane lining it and covering the glans will be found to be inflamed and often ulcerated in places. The inflammation may become so intense as to cause gangrene. This is generally limited to the prepuce, but may involve a considerable portion of the integument of the penis.

Phimosis is always present in some degree, whilst in a repeatedly recurrent case it is well marked owing to the thickening and contraction of the preputial tissues. Forcible retraction of such a foreskin over the glans is likely to result in paraphimosis. The constricted orifice of the prepuce tightly encircles the glans, and obstructs the return of the blood by the veins. This causes the end of the penis to swell, and the mucous membrane of the foreskin which lies in front of the constricting ring becomes greatly distended with serous exudation, and may, if unrelieved, become gangrenous.

Treatment.—Several times a day the preputial sac should be gently cleansed from all secretion with warm water, and then irrigated with a mild astringent antiseptic solution, such as nitrate of silver (1 : 5,000). If the foreskin can be drawn back, a thin layer of gauze soaked in the lotion should be interposed between the glans and the prepuce. Later, when the secretion is lessened, the lotion may be replaced by an astringent dusting-powder, such as oxide of zinc. When the glans cannot be uncovered, the parts under the prepuce must be cleansed and irrigated by means of a wound syringe. If there be much œdema and cellulitis, evaporating lotions and wet dressings may be applied to the penis. In cases of severe cellulitis, where gangrene threatens, the prepuce should be circumcised or divided by a free dorsal incision.

PAPILLOMA

It frequently happens that numerous small warts develop on the mucous membrane and skin of the genitals of persons suffering from gonorrhœa. Such warts are due to the irritation of the skin and mucous membrane from the constant bathing with decomposing pus, especially gonorrhœal pus.

These warts most frequently grow from the mucous membrane covering the glans penis, especially about the corona, but they are also found on the integument of the penis, the scrotum, the anal region, and the inner part of the thighs, and occasionally within the urethral canal.

In the female they are met with springing from the mucous and cutaneous surface of the vulva and perineum. The warts may be single, but usually are multiple, and vary in size from a pin's head to large cauliflower-like growths. Their appearance and consistency differ considerably, according to their situation. If they are growing from the mucous membrane, where they are kept moist, the epithelium covering them is thin and delicate, so that they readily bleed on being touched. In drier situations they become covered with a hard and horny epithelium.

Histologically these growths are true papillomas. The papillæ of

the integument are greatly hypertrophied and œdematous, and are covered with a thickened layer of epithelium They therefore in no way structurally resemble the small-celled infiltration of the syphilitic condylomata with which they are sometimes confounded. Apart from the fact that they grow in situations where the integument is exposed to the irritating and macerating action of fetid discharges, their origin is not known. It has been supposed that the growth is the result of a specific micro-organism, but proof is wanting.

Treatment.—There is seldom any difficulty in effectually dealing with this condition. The cause of the irritating discharge must be treated and the affected part kept scrupulously clean. In many cases this is all that is necessary to cause the warts to shrivel up and disappear. If they persist they may be touched occasionally *with strong alcoholic solution of perchloride of mercury, and kept* dusted with an astringent powder, such as alum, oxide of zinc, or resorcin. Larger growths are best removed with the knife or scissors, and the base should be touched with the cautery to arrest the hæmorrhage.

INFLAMMATION OF COWPER'S GLANDS

Occasionally the small glands of Cowper, which are situated in the perineum on either side of the urethra, become inflamed An acute inflammation of one of these glands (for the disease is almost always unilateral) is a rare complication, but a systematic examination of the perineum will show that a mild catarrhal inflammation is not uncommon. The gland is best examined by the surgeon inserting the forefinger of his right hand into the rectum and palpating the perineum [illegible] ie patient should [illegible] By thus compressing the tissues of the perineum at the apex of the prostate gland any slight enlargement or tenderness of either gland is readily detected. When this happens it usually does so during an attack of acute gonorrhœa, and gives rise to a firm, painful swelling in the perineum, midway between the scrotum and the anus Should the inflammation proceed to the formation of an abscess, the swelling increases in size until it impedes, more or less, the passage of urine and renders defæcation painful The skin over the abscess becomes red and acutely tender, and if unrelieved, it generally bursts externally, but may do so into the urethra or, more rarely, into the rectum.

Treatment consists in the application of hot fomentations to the perineum to relieve the pain in the acute stages, and the free opening of the abscess from the perineum as soon as pus is detected. It is undesirable to delay the opening of these abscesses, as otherwise

they may burst into the urethra or rectum and give rise to troublesome sinuses. In the chronic form of the disease the contents of the gland are expressed by means of the finger, and that and the urethra are irrigated as in chronic prostatitis.

LYMPHANGITIS AND LYMPHADENITIS

In almost every case of acute gonorrhœa in which the symptoms are at all severe the *inguinal lymphatic glands will be found to be* slightly swollen and tender. Generally this lymphadenitis soon subsides, and hardly calls for special treatment, for the inflammation does not give rise to suppuration. Repeated bacteriological examination of the liquid, withdrawn by aspiration from such inflamed lymphatic glands, always fails to show the presence of the gonococcus. The lymphadenitis may or may not be accompanied by an inflammation of the cutaneous lymphatic vessels (lymphangitis) of the penis. When this is present, faint, thin, red lines are seen in the skin of the penis, running from the glans towards the pubes. If the penis be palpated, the inflamed lymphatic vessels can be felt as firm cords, about the size of a steel knitting-needle. The presence of these inflamed lymphatics may give rise to various distortions of the penis, as in chordee.

Treatment.—*Rest and the application of evaporating lotions*, or glycerine and belladonna, to the inflamed parts is, as a rule, all that is necessary in these cases. Should an abscess form, an incision to evacuate the pus is indicated.

EPIDIDYMITIS

Next to prostatitis, the most frequent complication of posterior urethritis is an inflammation of the epididymis. This complication occurs in from 10 to 30 per cent. of all cases of urethritis. *It is found*, as we might expect, far more commonly in hospital than in private practice. There can now be little doubt that epididymitis is due to a direct extension of the gonococcal inflammation of the posterior urethra by means of the vas deferens. In the majority of cases this *infection would seem to* be a *pure* gonococcal one, though it may be a mixed infection. The exciting cause of this disorder is to be sought in anything which may give rise to an exacerbation of the urethritis, and so further its extension to the posterior portion of *the urethra* Violent bodily exercise, alcoholic or sexual excess, instrumental examination, irritating injections, are all apt to be followed by the sudden development of epididymitis. By experiments upon dogs and rabbits (Oppenheim and Löw) it has been shown that, when the *colliculus seminalis is strongly irritated* by any means, antiperistaltic waves are produced in the vas deferens. These experiments fully explain how gonococci and other organisms can pass from the urethra

to the testicle against the normal direction of the current within the vas deferens.

Epididymitis most commonly develops during the second, third, or fourth week of a urethritis, that being the most usual time for posterior urethritis to appear; but it may occur at any period, from the earliest onset of the acute disorder to late in the chronic condition. It attacks either gland with almost equal frequency. In a small percentage of cases (5 per cent., Castelnau) both glands may be affected simultaneously; in other cases the testicles are attacked one after the other.

Symptoms.—The inflammation generally begins suddenly. The patient experiences pain, without any warning, in one of the testicles, which he finds to be swollen and acutely tender. Both the swelling and the pain rapidly increase. The inflammation is principally confined to the epididymis, more especially the globus minor, but the gland proper also suffers to a greater or less degree. A serous or seropurulent fluid, in which gonococci may often be detected, occupies the tunica vaginalis. If the inflammation is severe, the scrotal integuments become thickened and œdematous, the small folds obliterated, and the surface red and glistening. There is usually some amount of fever present, and nausea and even vomiting may be caused by the severity of the pain. This is the most severe when the spermatic cord is also involved in the inflammation (funiculitis) The acute attack reaches its height in from four to five days, and then soon begins to decline. The effusion into the tunica vaginalis becomes absorbed, and so considerably reduces the size of the scrotal swelling The swollen gland and epididymis slowly resume their natural size, though many weeks, or even months, may pass before this is completely effected

During the acute stage of the disease the urethral secretion greatly diminishes, so that the patient no longer notices its presence This fact, though well known, is a constant trap to the medical student, who diagnoses traumatic orchitis because the urethra is free from discharge. As the acuteness of the epididymitis subsides, the urethral secretion reappears.

Diagnosis.—It is but rarely that any difficulty is experienced in making the diagnosis of gonorrhœal epididymitis. The acuteness of the early symptoms distinguishes it from syphilitic or tuberculous lesions elsewhere; the character of the swelling is different, for the enlargement of the gland and epididymis in urethritis is of a smooth and uniform nature, whilst the tuberculous affection is generally limited to the epididymis, and is nodular in character. Syphilis usually attacks the organ proper, and is seldom confined to the epididymis. Perhaps the most frequent mistake made in diagnosis is the result

of accepting naïvely the patient's statement that the swelling is due to a knock or strain. All doubt as to the origin of the inflammation is generally settled at once by directing the patient to make water, preferably into two glasses, when the presence of pus, threads, or mucus in the urine will at once *proclaim its true nature.*

Treatment.—A point of primary importance to be observed at the onset of epididymitis is that all local treatment of the urethritis must be at once suspended. While this complication is in its acute stage all injections or other topical applications will only aggravate the trouble. *Even when the pain has gone and the swelling is disappearing,* it is a grave mistake to be in a hurry to recommence the local treatment. During the acute stages we must rely upon the internal administration of the balsams or, better, salicylate of soda, in order favourably to influence the urethral inflammation.

Whenever practicable the patient should be kept in bed, and in any case the testicle should be supported by a well-fitting suspensory bandage provided with thigh-straps.

Under this treatment the acute symptoms generally abate within a few days. The pain and discomfort disappear, and the swelling *gradually subsides.* The absorption of the *inflammatory products* is materially hastened by gentle pressure applied to the part. At first this is best done by means of the suspensory bandage, but later, when all tenderness has disappeared and the swelling is limited to the epididymis, it is generally advised to apply the pressure by means *of firm strapping. It is, however, far from easy to strap a testicle* so as to obtain the right degree of pressure, and a well-applied bandage is quite as efficacious and much more agreeable to the patient.

Lastly, it must be remembered that the posterior urethritis which *gave rise to the epididymitis will require appropriate treatment.*

ACUTE PROSTATITIS

When in the course of an acute gonorrhœa the inflammation spreads to the posterior urethra (as it does usually about the end of the third week), it almost of necessity involves the prostatic gland, giving rise to a purulent catarrh of its numerous mucous follicles. This acute follicular or catarrhal prostatitis is limited to the mucous membrane, and gives rise to no symptoms beyond those of acute posterior *urethritis,* already described. Usually, under appropriate treatment, the inflammation readily subsides; but occasionally, in consequence, perhaps, of some indiscretion of diet or hygiene, the inflammatory action spreads to the interstitial substance of the prostate, and so gives rise to an acute diffuse or parenchymatous *prostatitis.* The *inflammation* spreads from the mucous membrane deep into the substance of the

prostate, and there, between the glandular elements, forms numerous small yellow infiltration foci, which either develop into minute miliary abscesses or coalesce so as to form one large collection of pus.

The **symptoms** evoked by an acute parenchymatous prostatitis vary according to the seat and severity of the inflammatory process. As a rule the onset is decidedly sudden, the patient experiencing a feeling of weight and uneasiness about the rectum and perineum, as though there were a foreign body in the bowel, the desire for micturition becomes distressingly frequent, though the urine is passed with increasing difficulty and pain; retention of urine is not uncommon, and should always arouse the suspicion that an abscess has developed. The temperature rises rapidly, and general feverish symptoms are present. *Per rectum* the prostate can be felt to be greatly swollen, hot, and acutely tender. Under appropriate treatment the inflammation usually resolves, but occasionally proceeds to suppuration, and the abscess, if untreated, after a longer or shorter time bursts into the urethra or rectum, or, rarely, opens externally through the perineum.

Treatment.—As soon as this complication is suspected all local treatment of the urethritis must be suspended; the patient must be kept in bed, on a low diet, and the congestion of the lower part of the bowel relieved by a mild purgative. For the relief of the pain and tenesmus, heat should be applied to the perineum by means of large poultices or frequent sitz-baths, or hot-water enemata may be given. For severe pain belladonna or heroin (gr. $\frac{1}{6}$) suppositories are valuable. If the urinary retention persists in spite of morphia and hot applications, the water must be drawn off with a soft rubber catheter As soon as an abscess is detected it should be opened, the incision being made through the perineum by choice, though, should the abscess point toward the rectum, it may be opened there without fear of septic or other complications following.

CHRONIC PROSTATITIS

It is necessary now to draw attention to this frequent and serious complication, a condition which has, perhaps, more influence in keeping up the chronic urethritis than any yet discussed. Chronic prostatitis generally develops insidiously during the course of a chronic urethritis, less frequently as the continuation of an acute prostatitis It arises as one of the consequences of the gonorrhœa spreading to the posterior urethra and infecting the prostatic glands. A chronic desquamative catarrh of these glands is set up, which has little or no tendency either to spread to the parenchyma of the prostate or to form an abscess.

The importance of this disease lies not so much in the symptoms

it creates as in the difficulty with which it is eradicated. Long after the gonococci have disappeared from the urethral secretion they can from time to time be found in the expressed prostatic secretion, and so long as a focus of gonorrhœal inflammation persists in the prostate, the patient is naturally liable to a recurrence of the urethritis.

Symptoms.—Chronic catarrhal prostatitis often gives rise to no *very characteristic subjective symptoms. The patient usually presents* the ordinary symptoms of chronic posterior urethritis—a slightly increased frequency of micturition, some sexual irritability or disturbance, and a feeling of weight or oppression about the neck of the bladder. Threads may be traced in the second portion of the urine. Often the most marked symptom is a grave disturbance of the general

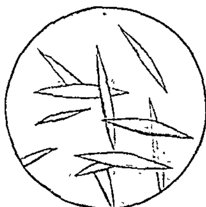


Fig. 224.—Charcot's crystals.

nervous system. The patient becomes hypochondriacal, and highly exaggerates his symptoms and the severity of his complaint, and he is very apt to develop into a chronic sexual neurasthenic.

All subjective symptoms may, however, be, and frequently are, entirely absent; and it is not until the prostatic secretion is examined that the disease is recognized. For the purpose of microscopical examination the prostatic fluid is best obtained by first instructing the patient to pass water, so as thoroughly to clear the urethra from its secretion, then while the patient kneels on a couch, the surgeon gently strokes the prostate from behind forwards with the index finger, protected by a rubber glove. The prostatic fluid pressed from the gland passes down the urethra, and is collected at the meatus in a watch-glass. A characteristic feature of the prostatic fluid is the presence of long needle- or whetstone-shaped crystals, the so-called sperm crystals of Böttcher or Charcot (Fig. 224).

Should the prostate be inflamed, in addition to the normal cellular

bodies there will be seen pus cells in large and overwhelming numbers, and perhaps micro-organisms will be present also.

Treatment.—The treatment for chronic prostatitis is the same as that for chronic posterior urethritis, with certain additional measures. First and foremost is the systematic and gentle massage of the prostate twice or thrice a week. Following the massage, irrigations or instillations of astringent lotions are to be given. This massage of the gland, followed by astringent irrigations, is the cardinal treatment for chronic prostatitis. There are, however, certain subsidiary measures which may be employed with advantage, such as the use of small rectal injections of iodide of potassium, the internal administration of ergot, and the employment of ichthyol in the form of suppositories

SPERMATO-CYSTITIS

Two forms of the disease are recognized—(1) an acute inflammatory, and (2) a chronic catarrhal spermato-cystitis.

1. Acute Spermato-Cystitis

The acute form may develop at any period in the course of a posterior urethritis, the infection spreading along the ejaculatory duct to the mucous membrane lining the seminal vesicle. An acute catarrhal inflammation is set up, and the vesicle becomes distended with a muco-purulent secretion; this, in favourable circumstances, may proceed to the formation of matter—empyema of the vesicle—which, if unopened, may burst into the urethra, rectum, bladder or, rarely, into the peritoneal cavity. Generally, however, the catarrhal condition does not proceed to the formation of an abscess, but either resolves completely or, more frequently, passes into the chronic catarrhal condition.

Symptoms.—The most typical symptom is the frequent and often painful emission of sanguineous and purulent seminal fluid, which leaves grey spots on the linen, surrounded by a yellow or brown ring. Apart from this, the symptoms are not very characteristic, and are common to acute posterior urethritis and prostatic abscess, viz., frequent painful micturition, accompanied by much bladder and rectal tenesmus, and a feeling of the presence of a foreign body in the rectum, also increased sexual excitability, accompanied by priapism and the above-mentioned seminal emissions. On examination *per rectum*, a tender, fluctuating, sausage-like swelling can be felt above the prostate in the situation of the vesicle. Pressure on the swelling expresses *per urethram* a mixture of pus and semen, which, when microscopically examined, shows the presence of spermatozoa, leucocytes, and gonococci, and often other pyogenetic organisms. On this examination the diagnosis of acute spermato-cystitis rests.

2 Chronic Catarrhal Spermato-Cystitis

This condition, again, can hardly ever be diagnosed by the subjective symptoms alone, as they are merely those of chronic posterior urethritis, nor does a simple digital examination of the rectum afford much help, as the vesiculæ are seldom notably indurated or enlarged. The diagnosis is made or excluded by the careful microscopic examination of the expressed contents of the vesiculæ.

Treatment.—The treatment of spermato-cystitis, whether in the acute or chronic condition, is almost identical with that of prostatitis in the corresponding stage Thus, the acute condition is treated by rest in bed, light diet, and gentle purgation. The urine is kept acid and antiseptic by the internal administration of such drugs as salicylate of soda or salol. The painful bladder and rectal tenesmus is relieved by hot-water enemata and sitz-baths, and by the use of belladonna suppositories Should an abscess form, it must be freely opened, preferably from the perineum, by a pararectal incision.

In the subacute and chronic stages the massage of the vesiculæ and prostate two or three times a week is indicated, to be followed by urethral irrigation with mild antiseptic and astringent solutions. Later, iodide of potassium or ichthyol suppositories may be used to promote absorption of the inflammatory induration.

CYSTITIS

When the inflammation spreads to the posterior portion of the urethra it does not stop abruptly at the vesical sphincter, but to some extent affects the lowest portion, or so-called neck, of the bladder. In consequence many authors prefer to call posterior urethritis "urethro-cystitis." Such an inflammation of the bladder is, as we have seen, very common, and has been described fully in the section on Posterior Urethritis. A cystitis apart from this—that is to say, in which the whole or greater part of the mucous membrane of the bladder is involved —is not, as it is commonly believed to be, a common complication of gonorrhœa and, as its symptoms and treatment are practically those of posterior urethritis, it is unnecessary to describe it further here.

NEPHRITIS

An inflammation of the kidney arises occasionally in connexion with urethritis, either in its acute or its chronic stage. This may be brought about through a metastatic deposit in the kidney tissue or as an ascending inflammation from the bladder by means of the ureter, the latter being probably the more usual. This ascending infection—whether caused by the gonococcus or any other micro-organism, may be

due either to inflammation spreading by continuity from the bladder along the mucous membrane of the ureter till it reaches the pelvis of the kidney, or, probably far more frequently, to the micro-organism being carried directly to the kidney through anti-peristaltic contractions of the ureter. Gonococcal nephritis is a complication which is frequently overlooked. It is considered in the article on the Upper and Lower Urinary Tract, in Vol II.

GONORRHŒA RECTALIS

The mucous membrane of the rectum is occasionally the seat of a gonorrhœal inflammation This is far more frequent in the female than in the male, and is generally due to a lack of cleanliness on the part of the patient, causing the anal mucous membrane to become contaminated by the urethral discharge. The symptoms begin with a sense of heat and discomfort about the anus ; the mucous membrane becomes swollen and prolapsed and, at a later period, is often excoriated and deeply fissured The inflammation shows no tendency to spread up the bowel, and indeed it rarely extends above the sphincteric area The mucous membrane only is affected, and complications such as stricture of the bowel, contrary to what is generally believed, are rare The diagnosis rests upon the detection of the gonococcus in the pus.

Treatment.—In the acute stage the bowel should be cleansed with warm, mild antiseptic solutions, such as protargol and permanganate of potash, and the pain relieved by anodyne suppositories. In the chronic form, injections of nitrate of silver (1 : 1,000) or protargol (1 per cent) solution, or the insertion of astringent suppositories, are indicated.

CONJUNCTIVITIS

Some mention must be made, for the sake of completeness, of the above serious complication , for further details the reader is referred to the special textbooks on the diseases of the eye.

The disease most frequently attacks the new-born infant (ophthalmia neonatorum), infection taking place at the time of birth from some vaginal secretion of the mother finding its way into the infant's eyes. More rarely the eye, either of the child or of an adult, becomes infected by specific pus being conveyed by a dirty finger, sponge, etc. (ophthalmia gonorrhoica adultorum). Whatever be the mode of infection, the disease manifests itself after a period of incubation of from two to five days The conjunctiva becomes infected, swollen and œdematous, and secretes a profuse purulent and highly infective discharge. The disease runs a far more serious course in the adult than in the infant, and is capable of completely destroying the sight

of the eye within a few days, blindness being occasioned through perforation or sloughing of the cornea.

Treatment.—When the disease has once appeared it must be combated by means of antiseptic lotions, introduced after all purulent matter has been washed away by a stream of boiled water. The silver preparations are generally the most efficacious, either in the form of silver nitrate or protargol. When strong solutions are used they are best applied to the conjunctiva by means of a small brush, to avoid injury to the cornea.

The prophylaxis of ophthalmia neonatorum is of great importance and should form part of the routine of midwifery practice. The face and eyes of every infant immediately after birth should be carefully cleansed and a few drops of an antiseptic, such as a 2-per-cent. solution of nitrate of silver, instilled into each eye. Happily such simple measures are most efficacious, and would, if universally adopted, save countless eyes from destruction.

In all cases of gonorrhœa it is the duty of the surgeon to explain to his patient the necessity for scrupulous cleanliness, on account of the infectivity of the discharge. Should, however, a patient accidentally infect one of his eyes, steps should at once be taken to protect the other eye from the grave risk of contamination, by means of a Buller's shield or other dressing.

GONORRHŒAL METASTASES

Metastatic deposits, in consequence of the cocci escaping into the general circulation, may occur at almost any period of the disorder, either in the acute or the chronic condition. Most frequently they are met with in about the third week of the disease—that is to say, at about the time when posterior urethritis most commonly develops.

GONORRHŒAL RHEUMATISM

Metastatic inflammatory changes in synovial and fibrous structures such as the synovial membranes, ligaments and periarticular *fasciæ* of the larger joints, the special bands of fasciæ such as the plantar ligaments or the ilio-tibial band, and the sheaths of nerves, are especially common, and have been grouped together under the vague but convenient term "gonorrhœal rheumatism"

Gonorrhœal arthritis is the most common variety of metastatic inflammation; the infection as a rule is purely gonococcal, though at times other septic organisms may be present, more especially the staphylococcus. This rheumatic complication is found in about 2 per cent. of all cases of urethritis, and is especially liable to begin about the third or fourth week of the discharge. It has a curious and marked

tendency to affect women more than men, and certain joints more than others. This is well shown in the following table, recorded by Finger from 376 cases :—

Knee	136	Elbow	25
Ankle	59	Shoulder	24
Wrist	43	Hip	18
Fingers	35	Jaw	14
Other joints	22		

Unlike true rheumatism, gonorrhœal rheumatism rarely attacks more than one or two joints at the same time.

The inflammation develops suddenly in most cases; the joint, which was apparently perfectly well a few hours before, suddenly becomes painful, swollen and distended with a slightly turbid serous exudation, which under certain conditions may become purulent. In other cases the intra-articular effusion is comparatively slight as compared with the œdema of the periarticular structures. The skin over the joint is rarely reddened or œdematous. The exudation fluid in the joint undergoes gradual absorption, though occasionally it may last as a troublesome chronic serous exudation

Frequently the arthritis leads to a partial or complete ankylosis of the joint. A rare and very grave development is the occurrence of suppuration; such cases are almost always the result of a mixed infection of the joint, the gonococcus being associated with the staphylococcus or other pyogenetic organism It is characteristic of this form of rheumatism that the inflammation does not wander from joint to joint, but remains in that which is first affected, though others may subsequently become inflamed. Other gonorrhœal inflammatory troubles not infrequently develop during the rheumatic attack, such as endocarditis, iritis and cyclitis, neuritis (more especially in the form of sciatica), tenosynovitis, and myositis.

Prognosis.—The prognosis is good in general, though recovery is slow and recurrence of the inflammation is readily caused by slight injuries The effusion into the joint gradually becomes absorbed, and the joint regains its free movement. Yet it should be remembered that there is the possibility of some stiffness or ankylosis following, or else of an incomplete disappearance of the fluid and a chronic hydrops of the joint

Treatment.—The treatment of gonorrhœal synovitis is usually conducted on general surgical lines, as in other forms of acute synovitis —rest and fixation of the joint by means of light, well-padded splints, and anodyne applications to relieve the pain during the acute stage. Later, massage and gentle pressure to the joint by means of strapping

or bandaging are useful in assisting the complete absorption of the fluid and in preventing stiffness. Should suppuration take place the joint must be freely opened and drained. In many cases, however, better results are obtained by the use of Bier's hyperæmic treatment, both as regards the relief of pain, the reduction of the inflammation, and the prevention of the joint-stiffness. The urethritis should be treated according to its condition at the time, especial care being taken to avoid provoking an exacerbation by heroic measures.

Many authorities regard the subacute and chronic cases of arthritis as especially suitable for the vaccine treatment. Personally I have not had much success with this form of treatment.

ENDOCARDITIS

Next to the joints, the part of the body most frequently affected by metastatic infection is the heart. In such cases it will be usually found that the aortic valves are more frequently attacked than the mitral. Symptomatically there is little to distinguish such cases of endo- or peri-carditis from a like affection due to other septic organisms, and the true origin of the inflammation can only be inferred from its onset during an attack of urethritis. In all save the mildest cases the prognosis is extremely grave, death generally taking place within a few weeks The accuracy of this diagnosis can naturally only be ascertained by a bacteriological examination after death.

It is here unnecessary to discuss the subject at greater length Recent investigations have shown that metastatic deposits of *gonococci* occur far more frequently than has hitherto been supposed *in other parts of the body*, giving rise to various forms of inflammation, such as *pleurisy, peritonitis, meningitis, iritis, periostitis*, osteo-myelitis, cellulitis, etc. Such inflammations present no characteristic symptoms, and their true origin can only be traced by careful bacteriological examination.

Lastly, there are certain nerve lesions attributable to the gonococcus, such as myelitis and peripheral neuritis. It is at present uncertain how far these are due to metastatic infection or to the circulation of the toxin in the blood.

PROOF OF THE CURE OF GONORRHŒA: ITS BEARING ON MARRIAGE

One of the difficulties in the treatment of this disease arises from the fact that the patient is very apt to regard himself as restored *to health* long before a cure has been effected. While the disease is in the acute or subacute stage there is little likelihood of either doctor or patient

regarding it as cured. It is in the terminal stage alone that the difficulty of deciding arises. Here the difficulty may be very great, and the decision arrived at of much moment to the patient. It may not merely involve the question whether it is necessary for him to continue the treatment or not, but also whether he is entirely free from infection and therefore in a fit state for marriage.

For the confident determination of the important question whether a supposed cure is actual or not, and whether the patient may marry without fear of infecting his wife, a most careful and systematic examination of the patient is necessary; no value whatever must be placed on his assertion, however confidently made, that all discharge has completely ceased. So long as the gonococcus is present in the urethral secretion or in the mucous membrane there can be no question of the patient's infectivity or of his need for further treatment. At the same time, it must be noted that the detection of the gonococcus in the later stages of urethritis is far from easy, and that it demands considerable experience and patience. In this stage the micro-organism is present in very spare numbers, and is no longer found in its characteristic situation within the body of the leucocyte, as in the acute stage. Confusion as to the identity of the organism is much more likely to occur in such circumstances than in the earlier stages of the attack, and all the resources of bacteriology may have to be invoked to establish the diagnosis. Further, it frequently happens that the organism is absent from the secretion for days, and even weeks, together, and only reappears when the urethra is unusually stimulated from any cause, as sexual excitement or indulgence in alcohol.

In the intervals the micro-organisms may be lying *perdu* in some of the numerous crypts and follicles with which the urethra abounds. Hence, when attempting to decide whether the gonococcus is still present or not, it is necessary not only repeatedly to examine the secretion at intervals, but also to take such steps as will induce a certain stimulation of the tract (for example, the injection of nitrate-of-silver solution or the passage of a large bougie), and to pay special attention to the contents of the seminal vesicles, the prostatic and urethral glands. Nor is it wise to rely solely on the negative evidence of the bacteriological examination, no matter how thoroughly it may have been made; due consideration must also be given to other factors, such as the character of the urinary threads and the appearance of the mucous membrane, as shown by the urethroscope. As long as the threads are largely composed of pus cells, one is justified in suspecting that the gonococcus still lurks somewhere in the urethra. Before the surgeon can confidently assert that the patient is no longer infective, not only must the gonococcus be absent from the secretion, but also the mucous membrane must have regained its normal bright, glistening

appearance; its longitudinal folds must be clearly defined, and it must be free from all inflammatory areas.

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YAWS—TROPICAL SORE—LEPROSY—MADURA FOOT—GRANULOMA OF THE PUDENDA

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YAWS (FRAMBŒSIA TROPICA)

A SPECIFIC endemic disease limited to certain parts of the tropics, and characterized by a more or less abundant frambœsial eruption appearing in crops for one year or more. Tertiary manifestations may occur. Constitutional disturbance is rarely serious, and the mortality, except in very young children, is nil.

Geographical distribution.—The disease occurs in tropical Africa, and is especially common on the West Coast. It is also common in many of the West India Islands, and was probably imported there by slaves from Africa. In Fiji and most of the Pacific islands it is indigenous and known as "*Coko*" (*Thokŏ*). It occurs among the aborigines in the Malay Peninsula and Archipelago, and is there called *Purru*, and in Ceylon *Parangi*. In Assam and in Southern India local outbreaks have been recorded. Probably in these places the disease has been introduced by returned immigrants from the West Indies or other countries where the disease is now endemic.

Etiology.—No races are exempt, but the disease is rare among Europeans, unless they associate with the natives and adopt their methods of life.

In countries where the disease is indigenous it is practically confined to the children, but susceptible adults imported into such a country are frequently attacked. One attack protects for life, in the majority of cases.

The disease is due to a spironema, *Sp. pertenue*, closely resembling *Sp. pallidum*, and is spread from man to man by direct contact, or by contact with clothes, bedding, food, etc., fouled by the discharges from another patient; it may also be carried by flies or chigoes from one person to another.

In most cases the seat of inoculation is an ulcer or wound or other breach of the healthy skin or mucosa, and, though it may occur in any part of the body, in children it is usually near the mouth.

Morbid anatomy.—The lesions are those of a vascular subcutaneous granuloma. The skin overlying the growths is softened, and keratinization is imperfect. The epithelial scales and serous discharges form a crust, which is frequently sulphur-yellow in colour. Between this crust and the granuloma there is often some accumulation of a milky fluid.

Clinical appearance.—The lesion appears first as a pimple, which rapidly increases in size until it is about as large as a threepenny bit; it is well raised above the surrounding skin or projects from the edge of the infected ulcer. Shortly afterwards other nodules form, usually on the face, the back, or the extensor aspect of the elbows. They may number only three or four, or they may be very numerous (Fig. 225). Successive crops develop, the older ones subsiding, until gradually the newly formed yaws become more scanty and finally cease to appear. The later ones are often formed under the thick epidermis of the palms or soles, and in such situations are known as "crab yaws." These are very painful.



Fig. 225.—Case of yaws.
(*Journal of Tropical Medicine*)

Secondary ulceration, either superficial or deep, of the granuloma may occur, but is exceptional. In parts subjected to friction or to constant movement, as at the angle of the mouth, secondary ulceration is more common. Tertiary lesions have also been described, and even quaternary, the latter closely resembling parasyphilitic conditions. Further work, however, is required on the differentiation of these late lesions from syphilis.

Differential diagnosis.—At the commencement of the general eruption there may be considerable fever, and pains in the back and loins, so that when the eruption first appears it may for a day or two be confounded with *variola*.

After the first few days the disease may be confused with various cutaneous *syphilides*, especially in view of the fact that a positive reaction to the Wassermann test is obtained in yaws as well as in syphilis. From rupia it can be readily distinguished by the uni-

formity of the scabs, their yellow colour, and by the fact that, when one is removed, instead of a deep ulcerated surface a raised mass of pink granulation tissue may be exposed. From the rare frambœsial syphilide it may be impossible to distinguish a case of yaws on a single examination. The past history and the future progress of the case, especially as regards treatment, will distinguish the two diseases in most cases.

Taking the history of a case of yaws, one of the most striking *features throughout the whole course of the disease* is the essentially uniform appearance of the eruption, which is thus distinguishable from the polymorphic rashes of syphilis. The mucous surfaces are very rarely implicated in yaws during the early stages of the disease.

Prognosis is good as regards life, except in very young children. The disease runs a slow course, and may induce a certain amount of debility. In a small proportion of cases, deeper ulcerative lesions about the naso-pharynx and a lupoid ulceration of the face occur. These are by many considered to be tertiary manifestations of yaws, by others to be really syphilitic manifestations, and by yet others are described as a separate disease (*see* Guam Disease, p 890).

Treatment. 1 Prophylactic.—Cases of yaws should not be admitted into a general hospital, and should especially not be placed in a surgical ward, or in one where persons with ulcers are kept. Isolation of yaws is advisable, particularly in countries where it is not endemic. The spread of the disease since the abolition of slavery is probably due to the disuse of the yaws-houses.

Europeans probably owe their comparative immunity to the wearing of boots, to the covering of the greater part of the body with clothes, and to their habit of protecting small wounds and ulcerated surfaces, rather than to greater cleanliness.

European children should not be allowed to play about with native children, and should be especially warned not to share food, bananas, etc, with natives. Infection probably takes place in many cases by the interchange of half-eaten fruit.

2. Palliative and curative.—Ordinary cleanliness and good food tend to shorten the course of the disease, and, if anæmia exists, tonics of iron and arsenic are advisable. The functions of the skin should be stimulated by hot baths, warm drinks, and diaphoretic mixtures. After these measures have been adopted, the patient should be prepared for a novarsenobillon injection Such injections have a remarkable effect upon the disease, in many instances the one injection completely curing the condition For natives 0 4 grm. to 0 6 *grm is usually sufficient, with smaller doses in proportion* for children—under 3 years, 0·1 grm.; 3–10 years, 0 3 grm. If

necessary, a second injection may be given, or even a third, but, as already mentioned, one is usually enough—contrasting with syphilis, in which courses of eight to ten injections are now being given by many surgeons, with mercurial and iodide treatment in addition. Before the salvarsan days, mercury and iodides were employed in yaws, but were very uncertain in their action; there is now no necessity to use them. The salvarsan injections should be given intravenously in the usual manner. Where this is impossible, they may be given intramuscularly into the buttock, 0·4 grm. dissolved in oil.

GUAM DISEASE (PHARYNGITIS GANGRENOSA)

Guam disease is a progressive destructive ulceration of the nose, fauces, and lips. It resembles lupus, and usually commences inside the nares and extends over the face and along the mucosa to the fauces. In the extreme forms the bones and the hard palate are destroyed, as well as the soft parts.

The disease closely resembles that known in Fiji as Kanailoma, and is believed by many to be a tertiary manifestation of yaws. Others have supposed it to be a form of malignant syphilis.

TROPICAL SORE

(*Syn.*—Oriental Sore, Delhi Boil, Bouton de Baghdad, Baghdad Boil, Nile Boil, Local or Cutaneous Leishmaniasis, Date Boils, Aleppo Evil, Frontier Sore, etc.)

A chronic form of infectious ulceration met with in many parts of the tropics, but not evenly distributed. It is due to a leishmania, *Leishmania tropica*, and occurs in Algeria, Egypt, Arabia, Persia, Northern India, etc.

Infection is probably fly-borne (*phlebotomus*), though experimental proof of this is still lacking. In any district where the disease is endemic it is advisable to keep any minute ulcer or other breach of the skin covered. Similar ulcers occur in dogs.

Clinical appearances and pathology.—The ulcers and sores are usually on exposed parts of the body, the face, wrists, and ankles being most commonly affected. The incubation period may be a long one, for sometimes the sores do not appear for months after the patient's departure from an infected area. The lesion commences as a small red papule, which rapidly extends and in many instances forms an ulcer. In other cases the sore remains nodular, with no breaking down. Multiple sores may also be met with; they are characterized by their chronicity and by the thick crust which forms on their surface. If this crust be removed, some milky or serous fluid may be seen, and the floor of the ulcer, consisting of

flabby granulations, will be exposed. In scrapings of these granulations the broken-down tissue, on microscopical examination, shows bodies morphologically identical with those found in the spleen, liver, and elsewhere in kala-azar (Fig. 226). These non-flagellate bodies are the resting-forms of a flagellate organism, supposed by some to be a herpetomonas. In artificial culture they change shape, becoming elongated and each developing a flagellum.

Etiology.—As seen in the granuloma, the *Leishmania tropica* is recognized by having two masses of chromatin—one, the nucleus, large and not very rich in chromatin; the other, the micronucleus or centrosome, small, compact, and staining deeply with chromatin



Fig. 226.—Parasite of tropical sore in endothelial cell, with free forms.

stains. These two unequal chromatin masses are characteristic of the flagellates. The parasites are found in considerable numbers, usually enclosed in large mononuclear cells. They are 3–5 μ in average diameter, but are rarely spherical, more frequently they are oval, and may be pointed at both ends—oat-shaped. Leishman's or Giemsa's stain brings out the points of these parasites well, but carbol-fuchsin, diluted with three parts of water, is quite sufficient for their recognition. If this stain be used, the films must be fixed in alcohol, or alcohol and ether in equal parts, before they are stained.

Diagnosis, thus, is easy if microscopical examinations are made: without these it is difficult, though the chronicity, the thick crusts, the absence of deep ulceration, the raised, thickened edge, and the absence of purulent discharge should arouse suspicion. The parasites are best found in the spreading margins of the sore, and when searching for them a needle should be inserted through the skin here and some of the juice sucked up. Part of this is then spread

on a slide and suitably stained, while the remainder is used for inoculating hæmoglobin agar tubes (N.N.N. medium). In this way cultures of the parasite can be easily obtained.

Prognosis.—Spontaneous cure eventually takes place in all cases, but the ulcers may persist for a year, or even more. There is no danger to life, but the scars, though superficial, may leave unsightly marks, especially on the face.

Treatment.—Many drugs, chiefly of the nature of strong escharotics, have been recommended for the treatment of the ulcers. The application of such has often led to worse scarring than if natural healing had taken place. If the sore be small and just commencing, excision may be tried, and is often successful. Carbonic-acid snow, methlyene-blue powder, caustic potash, nitrate of mercury, potassium permanganate, iodine, protargol, and salvarsan are some of the many remedies that have been tried. Modern treatment consists in the application of tartar emetic intravenously, or as an ointment locally. The latter sometimes does very well, but if the sore is unbroken it is better to give the drug intravenously, commencing with $\frac{1}{2}$ gr. in 30 c c. sterile saline, and working up to $2\frac{1}{2}$ gr. as the maximum dose; 20 to 30 gr. in all may be required for cure. The sore should be protected suitably, and kept clean by some ordinary antiseptic lotion as well.

LOCALIZED EGYPTIAN LEISHMANIASIS (LEISHMAN NODULES)

Thomson and Balfour describe under the name of Leishman nodules a non-ulcerating skin disease which occurs in the Sudan, and in which are found bodies similar in many respects to those seen in tropical sore. Tumours form in the skin and appear as soft, pink, cheloid-like, raised growths, which are usually multiple and occur on the face, neck, shoulders, arms, and thighs. They commence as small points which increase in size; around these, fresh tumours appear and coalesce with the primary growth, so that large, irregular masses are formed. They do not ulcerate, but run a very chronic course and may persist for years. Madden states that similar growths are seen in Egypt, and that the Leishman-Donovan body has been found in them by Ferguson. He treats them by free and deep excision and subsequent skin-grafting.

AMERICAN DERMAL LEISHMANIASIS

Tropical sores of a similar nature to those just described have also been met with in South America under various names—Forest Yaws, *Pian Cayenne*, *Pian Bois*, *Bubas Braziliana*, etc. They are also due to leishmanial parasites, probably to another species, *L.*

americana. They are local at first, but may be followed by generalized infections (Muco-cutaneous Leishmaniasis), the parasites then attacking the buccal and oral mucosa and eating it away in much the same way as severe tertiary syphilis. The names of *Espundia* and *Uta* have been given to this condition.

Treatment.—This is similar to that of ordinary Eastern tropical sore described above, viz. by antimonium tartaratum injections intravenously. The treatment of the local sore should always be conducted as early as possible, and be very thorough (as much as 40 gr. of antimony in all), to prevent development of late lesions. When late lesions have appeared, antimony should also be given, but, though arresting the disease, it will not, of course, regenerate the destroyed tissues.

LEPROSY

Though formerly common in England and other temperate climates, leprosy is now met with as an indigenous disease in few places outside the tropics.

In the tropics it is widely distributed, and in most places is not only indigenous but of great antiquity. In some places, as in the Sandwich Islands and New Caledonia, it is either a recent importation or has at least only been common enough to attract attention within the last fifty years.

The manifestations may be divided into two great classes: (1) those in which the skin and mucous membranes are affected—tuberculate, nodular, or skin leprosy; (2) those in which the nerves are the main seat of the lesions—anæsthetic or nerve leprosy. Mixed cases are common.

Pathology.—The disease is due to an acid-fast bacillus, *B. lepræ* (p. 80), which closely resembles that of tuberculosis, though usually it is a little smaller. It may be as acid-fast as the tubercle bacillus, but in many cases is rather less so, and is decolorized with 25-per-cent acid more quickly than the latter It stains rather more readily. Several observers have recently claimed to have cultivated it, but there seems to be considerable doubt still amongst bacteriologists as to the validity of such claims. In the skin lesions of tuberculate leprosy it is very numerous and is usually found in small, dense clumps, in contradistinction to the tubercle bacillus, which is found with difficulty in such lesions.

Like most of the allied organisms, the lepra bacillus causes the formation of a round-celled growth or granuloma, but the amount of this growth is very small in relation to the number of bacilli found. The lepra granuloma is vascular, shows no tendency to suppuration or caseation, and does not contain giant cells.

Clinical appearances.—In **tuberculate leprosy** (Figs. 227, 228) there is either a diffuse infiltration of the skin and subcutaneous tissues, or definite nodules of various sizes are formed. Usually both conditions are present, so that the face and ears are swollen and covered with large and small tense nodules. The face and the ears are generally the earliest parts to be attacked, but the arms and other parts of the body may also be implicated. The hair falls out and the hair-roots are destroyed in the affected areas,



Fig. 227.—Tuberculate leprosy, mild manifestations.



Fig. 228.—Tuberculate leprosy, with unusually severe manifestations.

even when there are no visible tubercles. For this reason the hairs on the *eyebrows are often lost early in the disease.*

The mucous surfaces of the nose, pharynx, and larynx are often implicated, sometimes before there is much disease of the skin.

In the **anæsthetic type** one or more nerves in the body are affected. The ulnar nerve, or rather both ulnar nerves, and other *nerve-trunks that are subcutaneous in their course are most severely* affected. Loss of sensation and disturbed nutrition of the parts supplied by the affected nerve occur. Wasting of the deep muscles of the hand, and flexure contraction of the little and ring fingers (Fig. 229), may be the earliest sign of leprosy to attract attention, while, owing to the anæsthetic condition, *injuries and burns are frequent* and, when followed by ulceration, lead to complete destruction of the parts.

On the feet, and more rarely on the hands, perforating ulcers going right down to the bone are common.

In this form of leprosy there are anæsthetic areas on the skin in any part of the body, most common on the back or front of the trunk. These patches are of varying size, do not seem to be associated, as regards distribution, with any special nerves, but are always associated with changes in the appearance of the skin. Each is surrounded by a slightly congested zone, whilst in the centre the skin is discoloured and appears to be slightly pigmented in white patients, but slightly paler than the surrounding parts in coloured persons. The patches are absolutely anæsthetic in most cases, devoid of hair, and do not sweat. (Figs. 230, 231.)

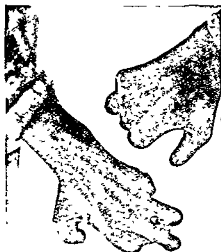


Fig. 229.—Hands in old case of anæsthetic leprosy.

The *Bacillus lepræ* has been seen in these patches by some observers, but in most cases it cannot be found, and therefore its absence does not aid in the diagnosis. The patches, however, cannot be due entirely to the nerve lesions, as no similar phenomenon is observable in other nerve lesions or as the result of injury to the nerves.

General symptoms.—Though the external manifestations and the anæsthesia naturally attract most attention, leprosy is a disease affecting the whole system. In the early stages there is often marked impairment of the general health, with febrile attacks, sometimes acute with a high temperature, sometimes with prolonged intermittent fever; whilst in other cases an irregular type of fever, with prolonged apyrexial intervals, occurs. The pyrexia is often, but not necessarily, associated with fresh external manifestations. If the disease is steadily progressive these febrile attacks may occur throughout its whole course. In most cases, after a time—usually two or three years—the disease progresses very slowly, or the condition becomes stationary; improvement and, in rare cases, spontaneous "cure" may take place, and, beyond the damage already done, no further change is seen. Even in these cases recrudescence may occur.

Differential diagnosis is not, as a rule, difficult. *Caries of the facial bones* may produce an appearance not unlike that of tuberculate leprosy, and *chronic streptococcic infection* or the results of repeated attacks of *erysipelas* may produce a thickening that is rather deceptive. The absence of the lepra bacilli from the fluid obtained

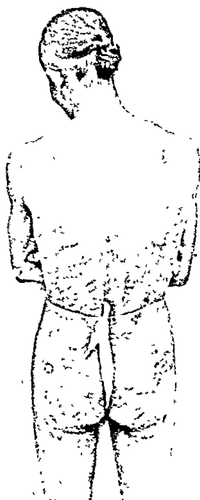


Fig. 230—Anæsthetic patches in nerve leprosy.

on puncturing the thickened areas, and from the mucous discharge from the nares, will be sufficient to exclude tuberculate leprosy.

The nerve or anæsthetic leprosy may be confused with conditions due to other nerve lesions, *syringomyelia* for example, which also produce wasting of the interossei, lead to the formation of perforating ulcers, or cause anæsthesia. The maculæ can usually be distinguished

from various rashes that resemble them, such as some *syphilides* and the rash in *trypanosomiasis*, by the anæsthesia (which is not always complete), by the absence of hairs, and by the absence of sweating in the maculæ after injection of pilocarpine. Lepra bacilli in these cases are sometimes found in the nasal mucus, but their absence does not negative the diagnosis of leprosy. Excision of a portion of the macula and examination of the tissue for the lepra bacilli is of little diagnostic value, as usually they cannot be found in this form of leprosy.

Prognosis.—Death occurs after variable periods. In the nodular form the prognosis is less favourable than in the anæsthetic, and death usually ensues in less than ten years after the onset of the disease, though when the disease becomes stationary the patient may live for thirty years or more. Intercurrent diseases, such as dysentery, chronic diarrhœa, tuberculosis, pneumonia, and Bright's disease, are the usual causes of death, but this may occur directly from the infection with the lepra bacillus becoming general and diffuse. In these cases the bacilli may be found in most of the organs, especially the liver, spleen, and testicles Gangrene—often as a result of injuries to the anæsthetic areas—necrosis, and amyloid degeneration are not infrequent causes of a fatal termination.



Fig. 231.—Anæsthetic patches in nerve leprosy.

Most cases of leprosy improve decidedly when the patients are well fed and well cared for. This is essential, whatever line of treatment be adopted.

Treatment.—Medicinal treatment must not be directed to the visible local lesions. The leprotic tissues are of low vitality, and escharotics and Röntgen rays simply cause extensive breaking-down of the tissues, with extensive ulceration The infected portions are so rarely limited to the skin that complete destruction is impossible, for the nodules in the submucosa cannot be destroyed. Such methods of treatment, therefore, substitute

an ulcer for a leproma, and cannot extirpate the whole of the disease.

Persistent use of chaulmoogra oil in doses of 5–30 minims or more, if the patient can take it, and of gurjun oil, has a beneficial effect in many cases. The doses should be steadily increased to the limit of tolerance. Recently Rogers has tried intravenous injections of sodium gynocardate (a product obtained from chaulmoogra oil) and claims good results. These may be combined with injections of sodium morrhuate intramuscularly, or the gynocardate may be given by the mouth and the sodium morrhuate intravenously. Intramuscular injections of perchloride of mercury in doses of ½ gr. every week have in some cases, particularly in England, had a beneficial result for a time. MacDonald and Dean recommend "Moogrol," an ethyl-ester of chaulmoogra oil. Iodicin, the mixed fatty acids, containing 2·5 per cent. of iodine, should be given simultaneously. Attempts have recently been made to obtain a vaccine from some of the cultivations of the so-called "leprosy bacillus." This line of treatment is still on trial. Whatever method of treatment is adopted, failures are more common than successes.

The perforating ulcers usually heal readily if they are deeply incised. The incision must completely divide the floor of the ulcer For gangrene or extensive necrosis, amputation of the affected part is the only measure; the wounds heal readily and the general health usually improves. Extensive operations can often be performed in lepers without anæsthetics. In the laryngeal affections, tracheotomy rarely causes any improvement, but may be necessary if the larynx is much involved.

MADURA FOOT (MYCETOMA)

A disease affecting usually the foot and ankle, rarely the hands or buttocks, and occurring in many parts of the tropics. In parts of India and in East Africa it is a common disease. It is rare in the West Indies, British Guiana, Cyprus, and the Malay States.

Etiology.—The organism causing the disease is a streptothrix which occurs in small nodules The free ends of the filaments become clubbed as in the actinomyces, *but the "clubs" are more spherical.* Several varieties are described corresponding to variations in the colour of the nodules, which in mass may be white, black, or pink, *or in the shape of the clubs. Brumpt describes seven in all.*

The streptothrix grows slowly on artificial media, forming small limpet-shaped masses. In culture it retains its stain when treated *by Gram's method.* It liquefies gelatin slowly.

Clinical features.—The affected parts become swollen, and riddled with sinuses leading deep into the tissues. From these sinuses

a thin watery or oily fluid exudes, in which granules of the *Streptothrix maduræ* may be found. The deeper parts are converted into

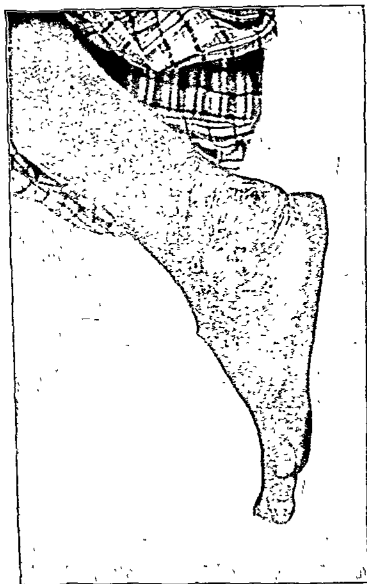


Fig. 232.—Mycetoma of about two years' standing.
(*After Legrain.*)

hard, fibrous tissue in which small granulomatous masses are situated; it is in these granulomas that the fungus grows.

The method of invasion is not known, but from the frequency with which the foot is affected it may be inferred that the infection usually takes place from some source in the ground. The strepto-

thrix, once introduced, spreads deeply, and ultimately invades t bones of the foot or ankle. The affected foot becomes quite useles the muscles of the leg and thigh atrophy, and the swollen, distort foot at the end of the withered limb makes an unmistakable clinic picture (Fig. 232). The disease lasts for years, progresses slowly, an shows no tendency to become generalized. Death usually occu not from the disease, but from intercurrent affections.

The **differential diagnosis** is easy if mycetoma is su pected; otherwise it may be mistaken for syphilis, or caries of th tarsal bones. The absence of any other evidence of *syphilis*, a nega tive Wassermann, and the negative results of antisyphilitic treat ment, will readily exclude the first. *Caries* is more difficult to exclude as the sinuses lead to the deeper parts of the limb, and therefor towards the bones A probe inserted along one of these sinuses passe over a dense, rough structure, and gives the impression of bein "gritty." If, as usually occurs, the bone is invaded, it will be found to be softened.

Examination of the discharge may disclose the presence of small granules, which on microscopic examination are found to have the typical appearance of a "ray fungus." If these granules are not found, *fragments of the streptothrix are usually to be discovered in the fluid.*

The **prognosis** as regards life is favourable. Spontaneous recovery or recovery under medical treatment never takes place.

Treatment.—Local measures, whether these consist of antiseptics, escharotics, or excision of the obviously diseased tissues or resections of joints, are useless. Amputation of the part of the limb affected, a few inches above the obviously diseased part, is the *only* treatment. The earlier it is performed the better, and no recurrence in the stump or elsewhere is to be feared. Potassium iodide, even in large doses, has not been found of any value.

GRANULOMA OF THE PUDENDA

Syn.—Serpiginous Ulceration of the Genitalia (MacLeod); Ulcerating Granuloma of the Pudenda (Galloway); Sclerosing Granuloma of the Pudenda (Daniels and Powell). Locally, in the West Indies, the affection is known as Groin Ulceration.

Geographical distribution.—This disease occurs in India, West Africa, British Guiana, and some of the West India Islands, whilst a similar disease, possibly the same, occurs in Northern Australia and Polynesia.

Pathology.—The growth is a chronic vascular granuloma with a special tendency to cause a deep formation of dense, fibrous tissue which is highly contractile. There is no tendency to suppuration, caseation, or any degeneration other than fibrosis.

In section the growths are seen to be very vascular and to lie upon a base of very dense, almost cartilaginous, fibrous tissue. The epithelial covering is mainly retained, but is devoid of pigment and soft and transparent, so that the red colour of the vascular granuloma can be seen through it. Microscopically, the growth is a typical vascular granuloma, mainly composed of round mononuclear cells with a relatively large nucleus. The vessels are much dilated and distended with blood. The epidermis overlying the growth, when intact, is thickened, while the distinction between the different layers is lost, and there is little or no keratinization. The papillæ are usually enlarged. The hair-follicles and sweat-glands are ultimately destroyed, but in the early stages the growth is more extensive and deeper round them. In a coloured person, at the edges of the growth there is an irregular deposit of pigment, but in the older parts no pigment is found The dense subjacent fibrous tissue usually contains islets of active granulomatous material.

In the superficial layers numerous organisms may be found, while the deeper parts are sterile as regards bacilli. Donovan, Cleland, Aragao, and South American observers claim that the disease is due to a germ to which Araujo has given the name of *Calymmatobacterium granulomatis*. Walker re-describes this organism as a capsulated intracellular diplococcus, probably the *Bacillus mucosus capsulatus* of Friedländer's group of bacilli. Wise in British Guiana has found spirochætes in the lesions.

The disease is acquired by sexual connexion, and is therefore in the venereal group

Clinical characteristics.—When the disease occurs on the skin the fibrous mass can be felt underneath the superficial part of the growth, which shows through the overlying non-pigmented and translucent, though thickened, skin as a red granulomatous mass.

Secondary superficial ulceration of the skin may occur, for the imperfect keratinization and sodden condition of the epithelium render it specially vulnerable. When the disease affects the mucous surfaces, ulceration takes place earlier and may extend deeply.

The disease runs a chronic course and does not directly affect the general health. Spontaneous cure by the complete conversion of the growth into dense fibrous tissue takes place but rarely. More commonly cicatrization occurs in parts, especially near the centre, while slow extension, by continuity or by auto-inoculation, goes on elsewhere along the moist folds of the skin. The rate of spread is variable, but the extension may continue for years. The first appearance is usually on the glans or the skin of the penis, and in the female on the labia. The growth extends rapidly on the glans or on the mucous aspect of the labia, but very slowly on the skin. It may

remain limited for years to these situations. Frequently, however, other growths appear in parts where the skin is usually soft and moist, and that are much in contact with the tip of the penis or with discharges from the labia.

In the male, therefore, the growths are usually found on the inner aspect of the groin or lower part of the abdomen (Fig. 233), and extend along the folds of the groin and the fold between the thigh and the scrotum. In old-standing cases they may spread over the perineum and round the anus to the tip of the coccyx (Plate 76).

In the female the main extension is backwards on the perineum,

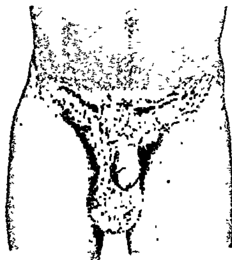


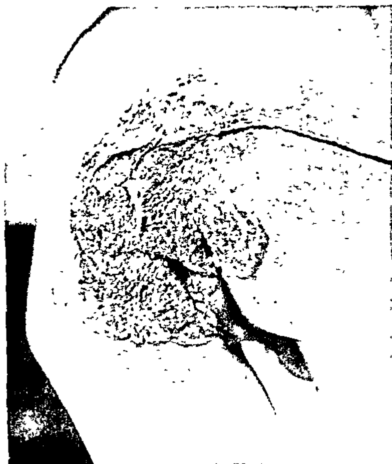
Fig. 233.—Granuloma of the pudenda in the male.

(*From "Manson's Tropical Diseases"*)

but sometimes, though more rarely, between the labia majora and the thighs anteriorly, so as to reach the mons veneris and thence the inguinal folds.

The growths, owing to the translucency of the skin, are red and are often mistaken for ulcers. Though there are no sweat-glands in the older growths, there is usually a profuse watery discharge, which may be very offensive. The granuloma is not painful. Extension up the mucous surfaces readily takes place, and causes serious trouble. The disease extends only a short distance up the urethra, but causes there a stricture of the meatus, which contracts rapidly after dilatation. It passes some inches up the rectum, and there gives rise to a true ulceration of the mucosa and a cicatricial narrowing.

In the female it rapidly spreads up the vagina and sets up a chronic leucorrhœa. It does not invade the uterus. When, as frequently happens, both rectum and vagina are invaded, the



Ulcerating granuloma of the pudenda. (*McGavin's case.*)

PLATE 76.

septum often breaks down and incurable recto-vaginal fistulæ are formed.

Beyond the inconvenience, little trouble is caused unless the mucous surfaces are implicated.

Differential diagnosis.—When the disease is limited to the genitalia it requires careful diagnosis from *malignant disease* and *tertiary syphilides*, from which it may be differentiated by microscopical examination, Wassermann reaction, etc. When it occurs in the groin or on the perineum it must again be distinguished from the same diseases, and also from *lupus*.

Prognosis is favourable as regards life and general health Spontaneous cure by cicatrization occurs, but is rare. Large doses of potassium iodide in a few cases seem to aid the tendency to cicatrization; but such cases may have been syphilitic in nature. Where active treatment is impossible, recovery from the local conditions is exceptional.

Treatment. **Surgical.**—If complete excision of the growth and underlying sclerotic tissue be possible, it is effective. Scraping is of value, but usually there is recurrence from portions of the growth left in the dense fibrous tissue. If scraping be combined with escharotics the probability of recurrence is slightly less

Treatment by X-rays followed by scraping has in some cases proved highly successful.

The stricture of the urethra can be treated by amputation of the glans. For the recto-vaginal fistulæ, only palliative treatment is possible.

Medical.—Intravenous injections of tartar emetic (antimonium tartaratum) have recently been found to be specific for the disease. The antimony (sterilized by boiling) is given, in sterile saline or distilled water, directly into the veins. Great care should be taken that none leaks into the tissues, as otherwise sloughing and necrosis take place. It is usual to begin with a dose of ½ gr., this being increased each time by ½ gr. until the maximum dose of 2½ gr. is reached. The salt is best given well diluted, say in 30 c c. of saline, by the gravity method, and should be administered twice a week, though some observers now give similar injections in schistosomiasis every other day. Others prefer to inject the solution into the vein direct from a syringe, the salt being then diluted in 10 c.c. of saline. The treatment is continued until the lesions are healed. In a case treated by one of us (G. C. L.) a total of 53½ gr. was required before complete healing took place. A few cases appear to be refractory even to the antimony.

GLANDERS

By E. ROCK CARLING, B.S., F.R.C.S.

Glanders, the most dangerous of equine diseases, is a specific infection communicable to man and to some other animals.

Etiology.—Amongst human beings the disease is almost entirely confined to men Not more than 3 per cent. of the recorded cases are in *females*; the infection of children is a rare accident. The most important etiological factor is an occupation involving contact with diseased animals, their carcasses, or their immediate surroundings. Thus, grooms and coachmen, cavalrymen, veterinary surgeons, blacksmiths, and stablemen make up the bulk of the affected. Knackers, who are relatively exempt, sometimes exhibit, post mortem, signs which have been interpreted as indicating a latent form of the disorder

Infection occurs through the abraded skin, and possibly by the hair-follicles; through the nasal and buccal mucosa, by inhalation or by ingestion Blood-sucking flies may possibly be a medium of transmission

The period of incubation varies widely; the usual time is from two to eight days, but it may extend to three weeks, or even longer.

The characters of the specific micro-organism, the *Bacillus mallei*, are described on p. 81. The bacilli are generally scanty in the affected tissues, and even in the pus from acute abscesses may be very difficult to find.

The **initial lesion** is frequently overlooked, and there may be no recognizable signs for a considerable time, even months, after the actual infection. Invasion by the skin *usually occurs upon* an exposed part through some breach of surface; inoculation by scratching is occasionally observed. There is no typical chancre, but a papule may appear and quickly ulcerate, or the wound may develop erysipelatoid swelling with lymphangitis and adenitis. In some instances vesicles are noted round the point of entrance. In the case of the mucosæ of the mouth and nose the onset is usually with catarrh; a copious, *thin, sero-purulent, and later sanious, acrid* fluid flows from the nostrils, or is expectorated. Ulceration is the

rule, but is not invariable. Severe diarrhœa at the outset suggests infection by ingestion, but gastro-intestinal lesions in man are rare. Infection per vaginam is recorded (Auer)

Morbid anatomy.—*All the tissues of the body* are affected. The cutaneous lesions are papular, vesicular, and pustular eruptions, serpiginous ulceration, and local gangrene In the mucosæ there is destructive granulomatous ulceration, rapidly spreading, but with a tendency to heal Intra- and intermuscular abscesses are common; the contents are sometimes viscid detritus, yellow, red, grey, or brown in colour; pus is often thick or curdy. Periosteo-myelitis is not infrequent; when the bones of the calvarium are involved there is often an extradural abscess or pachymeningitis. Phlebitis and thrombosis are met with; whilst implication of the lymphatics, with development in their course—possibly at the valves—of nodular swellings which usually suppurate, is so characteristic that the name "farcy" has been applied to the type of case in which such subcutaneous nodes or "farcy buds" are a prominent feature The term is unnecessary and should be dropped At autopsy the liver, spleen, and kidneys fairly often show nodules or abscesses, the testicles but seldom The lungs generally exhibit patchy areas of pneumonic consolidation; extrapleural suppuration is not rare

The **histological** appearances resemble, for the most part, those met with *in the other granulomas, but vary considerably with the* virulence of the strain of bacillus concerned. Chromatotaxis is a prominent feature of the microscopic appearances

Clinical course.—For descriptive purposes it is usual to speak of "acute" and "chronic" glanders. If it be remembered that a common termination of the less severe form is in acute exacerbation, and that any lesion may occur in either type, this distinction may be preserved Chills, which are usual in the acute form, have also been noted about the time of infection, even in cases of many years' duration. Prostration, which is pronounced when the course is rapid, may also be a striking feature in the presence of a single isolated lesion, such as an intramuscular abscess. Lymphangitis and erysipelatoid tumidity, often noted about the wound of entrance, are also of common occurrence, especially about the face and neck, in the late stages of an acute attack (Fig 234). Broadly speaking, it may be said that the case which runs its course in a few weeks from the commencement resembles any other pyæmia. The character of the pyrexia, the malaise, the pains in the limbs, the delirium, the arthritis, the multiple abscesses, the pneumonia, and finally the generalized cutaneous eruption, which passes from papular to pustular or bullous —especially when these symptoms are combined with fetid catarrh of the upper respiratory mucosæ and tumefaction of the face—

present a clinical picture of *systemic infection* which only requires the history of *exposure to the glanderous contagion* to make the diagnosis strongly presumptive.

The lesions of the more chronic *type are protean. An indolent*, indurated ulcer of the hand or arm or leg, perhaps with hard *lymphatics* running from it, and associated *adenitis*; a *serpiginous, eroding ulcer*



Fig. 234.—Case of acute glanders.

that may lay bare a bone or open into a joint, or into the pleura. or into the trachea, and leave persistent sinuses; single or multiple inter- or intra-muscular abscesses, or periostitic suppuration or necrosis, or gangrene of the nose or palm or penis; purulent arthritis; purulent sinusitis; otitis media; conjunctivitis; dacryo-cystitis; bronchitis and pleurisy; jaundice and diarrhœa; or slow, destructive, polycyclical ulceration of the palate and fauces, with perforation into the nasal fossæ; necrosis of the septum, and disintegration *of the soft*

parts of the nose and lips—any of these may be present as the sole evidence of the disease; or, on the other hand, almost any combination of them may exist, or all in turn may figure in the clinical history of a case that spreads over, it may be, fifteen years, with intervals *of weeks or months or years of freedom from overt signs.*

Diagnosis.—It will be evident that while the multiplicity of the lesions, when of simultaneous occurrence, offers assistance to diagnosis, the diversity of the clinical picture in individual instances of a glanderous affection hinders recognition, and permits the true condition to be overlooked. The eruption has been mistaken for smallpox, varicella, impetigo, and herpes necrotica; the general febrile state for typhoid, typhus, influenza, acute rheumatism, and pneumonia.

The rash, which is irregularly distributed without regard to aspect, often comes out in crops over three or four days; it may be sparse and scattered, or close-set; the vivid red or purplish areola often noted around the vesicles and pustules is said to be characteristic (Pilcher)

The chronic lesions of the skin and mucous membranes may easily be confused with those of syphilis or tuberculosis, and even of lupus, actinomycosis, or leprosy.

The possibility of glanders should always be borne in mind in any case in which a patient whose occupation is likely to bring him into contact with sick horses presents a chronic inflammatory lesion of the skin, of the oral or nasal mucosæ, or an inflammatory mass in the subcutaneous or muscular tissues.

The mallein test, commonly applied to horses, may also be used in man. Small doses are unreliable, and 10–15 min have been given in many instances, even in the non-glanderous, without untoward effects. In the affected there is slight local reaction, the constitutional reaction is but little more than the pyrexia would account for; a maximum rise of temperature to 105° Fahr, with an average of 103 5°, returning to normal in about forty-eight hours, may be expected (Chart 5). Tuberculin does not produce a reaction in the glanderous. The method of cutaneous vaccination (von Pirquet's) has been successfully applied with mallein (Zieler and Martel).

Straus's test.—The most reliable, and in doubtful chronic cases the only reliable, diagnostic method is animal inoculation. An emulsion of suspected tissue, injected into the subcutaneous layer of the abdominal wall or into the peritoneal cavity of a young male guinea-pig, produces in from two to fourteen days, according to the virulence of the strain, an acute orchitis with engorgement of the tunica vaginalis, from which, to establish the proof, the *B. mallei* should be recoverable.

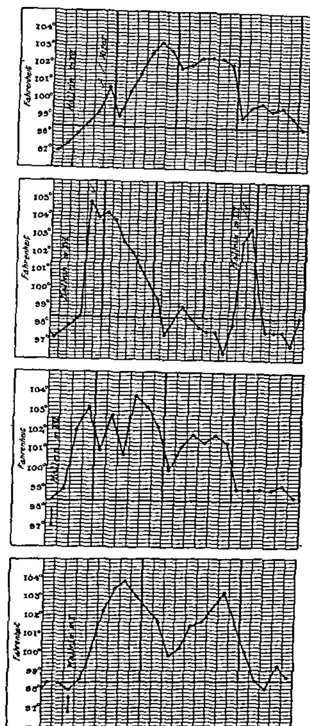


Chart 5.—Temperature of four cases of glanders in which mallein was used for diagnosis.

Examination of the blood is sometimes of value. The organism itself can, as a rule, be cultivated from the blood only shortly before death; the total and differential counts of leucocytes afford no evidence of special importance. With some infections, however, it is possible to demonstrate agglutination in dilutions of 1 in 100, whereas normal blood fails to agglutinate at a dilution of 1 in 25. The "complement-fixation" method holds out some promise of usefulness.

Treatment.—The various surgical measures of a regional character indicated by the occurrence of suppuration should be prosecuted with vigour. The local use of powerful antiseptics, such as pure phenol, seems to have been of definite value, but the only real hope of saving an acute case lies in methods addressed to the general defensive mechanism of the body, such as the injection of bovine or naturally immune serum, of which as much as

200 c.c. has been given at intervals within three weeks; or by the use of repeated doses of mallein, for which beneficial effects have been claimed. Some hope has been held out, by the publication of successful cases, that a vaccine may prove curative. This method should certainly receive a trial. Of drugs, mercury by inunction, potassium iodide, and aconite have been vaunted in the treatment of more chronic cases, but none has any specific action. Röntgen and other rays, and the various forms of electrical influence, have been employed, but without much success, for indolent lesions of the mouth and nose.

Prognosis.—It has been stated that 50 per cent. of the chronic cases get well (Sims Woodhead). This estimate is certainly much too high; 20 per cent. would be a closer approximation to the facts. Temporary recoveries may occur in the higher proportion, but many of them relapse, and not a few eventually succumb to the disease. The outlook in cases of pyæmic type, particularly when a generalized eruption has appeared, is gloomy in the extreme.

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ACTINOMYCOSIS

By C. C. CHOYCE, C.M.G.,C.B.E.,B.Sc., M.D.,F.R.C.S.

General description.—Actinomycosis is an infectious granuloma-forming disease due to invasion of the connective-tissue planes of the body or the internal organs by the actinomyces or ray fungus. Since its recognition in 1876 by Bollinger it has very frequently been found in herbivorous and omnivorous animals. In man it is considerably rarer, but less so than was formerly supposed. It was first recognized in England by Acland in 1884.

There is now no doubt that some of the cases which have been classed as actinomycosis, and which clinically more or less closely resemble it, are caused, not by the actinomyces, but by an allied organism of the same group—the streptotriches; this will account for the confusions in the description of the disease and for the frequent failures of the clinical pathologist to demonstrate the causative organism in suspected cases. Only by careful bacteriological examination can the identity of the causal organism be determined; similar streptotriches are to be found, for example, in the lungs and throat.

In streptothricial infections generally, and particularly in actinomycosis, the predominant characters are those of a chronic progressive granulomatous and fibrous infiltration of the connective tissues; this is accompanied by the development of multiple small abscesses, which discharge a viscid exudate, often but not always containing characteristic yellow or red granules composed of tangled masses of the fungus.

Frequently in the central parts near the original site of infection the disease displays a tendency to spontaneous cicatrization, synchronous with a slow centrifugal spread at the margins.

It is the cause of "wooden tongue" and "lumpy jaw" in cattle.

Colebrook differentiates four classes of cases, due to different types of organism, some of which are aerobic, such as that isolated in Boström's cases, and some anaerobic, such as the true actinomyces bovis described by Israel and Wolff. He classifies them thus—

(*a*) *True actinomycosis.*—Those that show granules composed of Gram-staining mycelium and from which the Actinomyces bovis[1] (Israel-Wolff) is isolated by culture. This streptothrix only grows at

[1] The word "bovis" must not be taken to imply that this organism is especially found in cattle, to the exclusion of other streptothricia.

body temperature and not at all at ordinary room temperature; it grows slowly in agar and only appears after from four to six days or longer; it does not grow on gelatin It is essentially anaerobic, although occasionally a thin growth is got under aerobic conditions. It does not sporulate, and dies out readily in culture. This group contains by far the greatest number of granule infections in man.

(b) "*Para-actinomycosis* (*Colebrook*)"—Those that show granules composed of Gram-staining mycelium, but that culturally differ from the Israel-Wolff type of organism.

(c) "*Actino-bacillosis* (*Lignières et Spitz*)."—Those showing granules composed not of mycelium but of bacilli.

(d) *A heterogeneous group of streptothricoses*, showing Gram-staining mycelial organisms, but the mycelium is not aggregated into granules visible with the naked eye.

Etiology.—The primary cause of true actinomycosis is the attack by the organism of Israel and Wolff, the characters of which have been described elsewhere (p. 103 and above), but many writers have included under the term the less common cases falling under Colebrook's last three headings.

In the discharge from the abscesses, or in a section of one of the granulomas, it typically appears as a number of small, scarcely visible, red, yellow, or grey granules (the so-called "red pepper" or "sulphur grains").

If a granule be floated out in water, it will frequently be found to consist of a central mycelium in which are entangled small round spore-like bodies. From this there radiate many fine threads, which may or may not show knobbed ends; in human cases of actinomycosis, knobs are often not observed, unless stained by special methods such as that of Wheal and Chown.

Following Boström (1891), it has usually been taught that the fungus is saprophytic, and probably dependent upon the presence of some particle of decaying vegetable matter lodged in a hollow tooth or other cranny. Its normal habitat is said to be inside the husks or sheaths of barley and other grasses.

Its *mode of ingress into animals* appears to be through abrasions in the mucous membrane, especially of the tongue, mouth, etc., due to scratches with infected grain. In *man* it is generally stated to gain entrance on particles of chewed grasses or inhaled grain-dust which become lodged in abrasions of the mucous membrane of the alimentary canal, in a tonsillar crypt, or in the hollow of a carious tooth. It seems probable that the presence of such a foreign particle is necessary for the initiation, if not for the progress, of the disease. Cases are recorded of infection by means of dental instruments and of splinters of wood.

Colebrook, however, points out that Boström's organism was not the anaerobic Actinomyces bovis that seems to be the common variety in man; that Harbitz has found the actinomycial types grown from straw to be bacillary aerobes: and that a delicate grower, like Actinomyces bovis, requiring body temperature for growth and not tending to sporulate, is unlikely to have a natural habitat outside an animal body. At the same time, it is certain that in many cases of true actinomycosis (Israel-Wolff type) foreign bodies have been found, e.g. in one of Colebrook's own cases, in one of Soltman's quoted by Poncet and Berard, and in others.

Although the infection usually occurs through the alimentary or respiratory tracts, the fungus may effect an entry through the skin or through the genito-urinary system.

In connexion with the relationship, first observed by Israel in 1878 and since then frequently confirmed, between actinomycosis and carious teeth, it is interesting to note that Lord has found, in the carious teeth of individuals without actinomycosis, organisms which have the morphology and staining reactions of actinomyces, and which have caused actinomycotic omental tumours in guinea-pigs inoculated with the contents of such teeth.

Predisposing factors.—These are:

1. Occupation. The disease is usually met with in men associated with the farming, stevedoring, and corn-chandlery industries.
2. The lodgment of a particle of grain.
3. Sex The affection is about twice as frequent in men as in women This is the commonly accepted statement based on former groups of cases, but Colebrook found it in his cases as common in women as in men, and in town dwellers as frequently as in agriculturists.
4. Age. Actinomycosis is commonest between the ages of 20 and 40.

Distribution of the lesions.—The fungus may attack any organ, but it shows a special tendency to spread in tissues of the connective-tissue type (areolar tissue, fibrous tissue, bones, and muscles). The commonest site in man is near the angle of the jaw; in cattle, in the tongue or jaw. Usually the disease first involves some part of the tongue, gastro-intestinal or respiratory tracts; but primary cases have been observed in the skin and the genito-urinary organs, e.g. in the kidney, prostate, and vagina. Secondarily, either by local spread or by metastasis, any tissue or organ may become involved—pleura, peritoneum, bones, liver, and even brain.

Schlange recorded 100 cases, of which 80 were in the jaw and neck The combined list of 430 cases collected by Illich in 1892,



Fig. 1.—Actinomyces in the human liver × 650

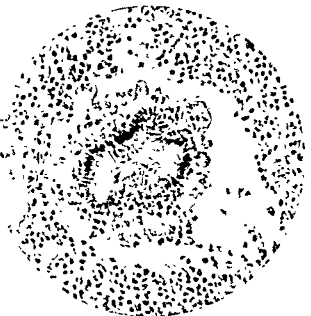


Fig. 2.—Actinomyces in tongue of cow. × 300

PLATE 77.

(Dr. J. M. Milne's cases.)

and Leith in 1894, shows the following distribution (Hurst has added 64 additional abdominal cases):—

Head and neck . .	224 }	55 75 per cent.
Tongue . .	16 }	
Abdomen . .	93 .	21 60 „
Lungs . . .	57 . .	13 25 „
Skin . .	11 . .	2·50 „
Doubtful	29 .	6 90 „
	430	100 „

Colebrook's 25 cases were classified thus —

Site	No.	Males	Females	Ultimate Result
Face and neck	10	7	3	9 cured, 1 died from cerebral abscess by direct extension through cranial base.
Thorax . .	8	5	3	7 died, 1 lost
Abdomen . .	6	1	5	5 died, 1 recovered
Dorsum of hand	1	1	–	Recovered completely.

These figures confirm the usual experience that (1) the disease is commonest in the face and neck, and (2) thoracic and abdominal cases are usually fatal. But both these opinions may be somewhat modified if Schlesinger's suggestion has weight, that some early cases arising in the appendix alone are probably cured by appendicectomy without being recognized.

Morbid anatomy.—At the site of infection there is a chronic inflammatory process, in which small round lymphocyte-like cells are usually seen. This area is soon surrounded by a firm fibro-cellular zone, and there ensues a gradual invasion of the neighbouring connective-tissue planes, with hard lumpy masses of chronic inflammatory material; this may take the form of a general diffuse brawny infiltration with ill-defined edges, or of a definite collection of tumours which display at first a smooth, regular surface and a dense, uniform consistency. Secondary pyogenetic infection is a common and, in internal organs, an outstanding feature; the abscesses burst and discharge the characteristic granular and viscid exudate, so that eventually there remains a widespread and sinus-riddled diffuse mass of nodular infiltration, with a more or less profuse purulent discharge.

Microscopic examination of a section shows a mycelium of radially arranged branching filaments lying in each softened area, and surrounded by a zone of fibro-cellular tissue. The sinus walls are lined by granulation tissue, which contains many "pepper granules." In the purulent contents of the abscesses, or in the discharge from the sinuses, the characteristic branching filaments are seen. (Plate 77, Fig 1.)

Colebrook suggests as a rough test that some suspected pus should be shaken vigorously in a test-tube with water: the ordinary pus elements are then broken up or emulsified; the actinomyces shreds, if present, are not fragmented and are seen, in holding up the tube to the light, as cream-coloured spherical bodies about ½–1 mm. in diameter, which quickly sink to the bottom of the tube.

On slightly squeezing such a granule between a microscope slide and cover-glass and examining unstained under a low-power objective, the characteristic "ray" formation of clubs may be seen between an outer shell of massed leucocytes and the inner core of the granule. On crushing further and staining, the core is seen to be composed *of a tangle of filaments*, which retain Gram's stain rather irregularly. But, in spite of this statement, the examiner must not be disappointed if he fails to find "clubs"; actual definite "clubs" are not usual in human cases. the granule being merely an irregular mass of filaments.

Clinical features.—The general symptoms are often *very vague unless an important organ be interfered with; so that*, if the disease be in an internal part of the body, diagnosis may be difficult until the tumour becomes large and palpable, or until the fungus is found in the sputum or other ejecta. The victim presents *slowly progressive weakness, anæmia, and wasting, often allied with* fever of a tuberculous type, and, when questioned, may give a history of employment involving the handling of corn or the inhalation of grain-dust. There is no tenderness, and may be no pain; when the latter exists, it is often neuralgic and due to pressure.

If the lesion is visible the conditions described under Morbid Anatomy appear, namely, a diffuse tumefaction of a firm infiltrating type, nodular in places, in others softening and exuding the "pepper granules" in a viscid and sometimes watery medium. The *overlying skin becomes mottled and purplish*. True suppuration and lymphatic adenitis are absent unless secondary infection by pyogenetic organisms has taken place.

The disease spreads by continuity, but occasionally invades a vein, and then may exhibit metastasis.

In special sites.—1. In the *head and neck*, which is by far the commonest seat of the disease, the infection nearly always commences from a carious tooth or from an abrasion of the mucous membrane. *Thence it spreads to the lower* jaw and cheek, though occasionally it may extend to the tongue, upper jaw, vertebral column, or even the base of the skull and brain. The disease pursues the course described above: multiple abscesses, discharging sticky exudate often containing "pepper granules," are formed in a mass of diffuse or nodular induration. Simultaneous cicatrization near the primary focus, and spread down the planes of the neck, occur, until perhaps, finally, the

disease reaches the mediastina, leaving behind it a dense, fibrous track of distorted and nodular scar. It may extend from one side of the neck to the other. Stiffness of the neck and difficulty in swallowing and breathing may result. The great vessels are surrounded, but usually escape, though Ponfick, Schlange, and others have recorded cases of erosion into the jugular veins and general metastatic actinomycotic "pyæmia."

If the disease enters at the angle of the mouth it may lead to very extensive deformity, as in a Chinese seen by the writer in 1908.

2. *The abdomen.*—In the alimentary tract below the pharynx, primary cases have been reported in the œsophagus by Mikulicz and others, but they are rare. Similarly, the stomach and small gut are relatively immune as compared with the large intestine. By far the greater proportion of gastro-intestinal cases occur in the region of the cæcum, appendix, and ascending colon. The chief growth is in the submucosa, where it commences as flattened, greyish nodules; owing to early secondary infection, softening and destruction are early and extensive. The peritoneum soon becomes involved. Dense adhesions form and become riddled by the disease, which thus, preceded by adhesions, spreads to all the surrounding structures and organs, penetrating any variety of tissue, even bone, until it may ultimately reach the abdominal wall and perforate it through many fistulæ. In like manner the abscesses may burst into the bladder, kidney, or pleura. Fæcal fistulæ are not infrequent, but intestinal obstruction is a rare sequel.

Clinically, the signs are, at first, malnutrition and secondary anæmia, sometimes irregular fever, and some intestinal catarrh, followed sooner or later by the discovery of a hard but ill-defined and usually painless tumour, which may show areas of semi-fluctuation. The cachexia becomes more marked, the irregular fever more constant, and later the lump may burst on the surface, usually in the cæcal region, and discharge the ray fungus. A comparatively frequent occurrence is that appendicectomy is performed for subacute appendicitis, the wound perhaps heals for a month or so, but then the patient returns with a mass in the ileo-cæcal region which is found to be actinomycotic; almost certainly the appendix was infected with the streptothrix from the beginning, but this fact was not recognized in the first instance. The liver is most frequently the seat of secondary deposits, which suppurate and give rise to irregular-shaped abscesses with walls of varying thickness. Local perihepatitis may occur.

3. *The respiratory tract.*—Lung infection may sometimes be primary and due to inhalation, or more usually secondary by direct spread from disease in the neck, mediastina, or abdomen. It manifests itself as a destructive broncho-pneumonia with peribronchial nodules and

small, softened areas often combined with interstitial fibrosis. In a few cases the fibrosis is the predominant character. During this earlier stage local physical signs are often wanting, and the general symptoms indeterminate. In a patient seen by McGavin and the writer, rapidly progressive emaciation and weakness were the only ascertained signs, until the chance expectoration of a single pellet containing the micro-organism led to a diagnosis. Later the lung becomes contracted, and the diameter of the chest on the affected side may be diminished. The disease extends to the pleura, giving rise to adhesions, and sometimes effusion. It eventually reaches and perforates the thoracic wall, diaphragm, or pericardium. In these later stages the temperature is higher and more constant. Pain, night-sweats, and repeated hæmoptysis may be present, and the physical signs of pulmonary disease are more obvious. The sputum contains granules of mycelium and evidences of lung necrosis, although elastic fibres are frequently absent. But in the lungs several streptotriches, other than those of true actinomycosis, may be found.

In the larynx, actinomycosis is usually secondary to disease in the neck or mouth, but cases have been recorded in which it appeared to be primary. It generally commences as a perichondritis.

4. The *genito-urinary tract* in any part may be secondarily involved in abdominal actinomycosis. Primary cases have been reported in the kidney, prostate, and vagina.

5. The *bones* are never the seat of primary actinomycosis. Those most commonly invaded secondarily are the lower jaw, vertebræ, ribs, and occasionally the upper jaw and the base of the skull. They undergo extensive erosion, which is not, as a rule, associated with any great amount of new periosteal bone-formation. In a few cases, however, this has been considerable. In the spine, angular curvature has been reported; the meninges and the cord usually escape, though there may be intercostal neuralgia.

6. Although the *skin* is more often secondarily than primarily involved, numerous cases are on record in which it was the initial site of infection.

7. In the *tongue* the disease takes the form of a dense fibrous infiltration ("wooden tongue" of cattle), with or without multiple nodules and abscesses. (Plate 77, Fig 2.) But this variety is very rare in man.

8. The *brain* may be invaded by metastatic deposits, carried to it by the *blood-vessels*, or, as in Ponfick's case, by spread from the cranial base. The abscesses are in the white matter, are usually [illegible]e, and are surrounded by areas of cerebritis and meningitis [illegible] velopment may be comparativel[illegible] and occupy only [illegible] eeks.

9. The *heart and pe*[illegible] be invaded [illegible] mycosis.

Diagnosis.—The disease must be differentiated from—(*a*) Tuberculosis, especially tuberculous lymphadenitis and periadenitis. (*b*) Carcinoma. (*c*) Sarcoma. (*d*) Syphilis. (*e*) Chronic abscess. (*f*) Chronic or subacute appendicitis in cæcal cases. (*g*) Chronic glanders of the skin and subcutaneous tissue. The following points will help in its differentiation.—

1. The history of great chronicity and exposure to infection.
2. The alternation of very dense infiltration with multiple semi-fluctuating areas.
3. The sinus-riddled condition, when present.
4. The gradual merging into the surrounding tissues.
5. The mottled bluish colour of the skin over the softened areas.
6. The fact that the lymph-glands are not affected unless secondary pyogenetic infection has supervened
7. The large size of the area involved compared with the small size of the tumour
8. The character of the exudate.
9. The diagnosis is rendered certain by the discovery of the characteristic organism in the discharges or in the granulation tissue.

A method of *serum diagnosis* depending upon fixation of the complement has been employed, but the results have been variable, the negative reaction being especially unreliable It is apt to give a negative reply in mild, though definite, cases.

Prognosis.—As regards life, the outlook is not so hopeless as is sometimes stated. Even untreated cases occasionally, though rarely, survive, and although the death-rate is high amongst patients subjected to treatment, a considerable number ultimately recover. The prognosis is worse if pyogenetic infection be added, if entrance into a vein and metastasis occur, if important organs become involved, or if amyloid degeneration follow as the result of infection with pyogenetic organisms. Death results from exhaustion, amyloid degeneration, or spread to a vital organ. The prognosis is worse in internal than in superficial cases, and is especially bad in thoracic cases.

The local lesions may persist for years, but if treated may ultimately heal with considerable deformity.

Treatment.—Chief reliance must be placed on the administration of large doses of potassium iodide, even more than 200 gr. per diem being necessary in many cases before any therapeutic effect is seen It may be given by mouth or by injection. The surgeon should be prepared for the pain and rise of temperature that may follow its exhibition, and should also give it in high dilution

Mercurial injections have sometimes caused apparent improvement. Injections of iodipin (1 per cent) have been useful in one of

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In the larynx, actinomycosis is usually secondary to disease in the neck or mouth, but cases have been recorded in which it appeared to be primary. It generally commences as a perichondritis.

4. The *genito-urinary tract* in any part may be secondarily involved in abdominal actinomycosis. Primary cases have been reported in the kidney, prostate, and vagina.

5. The *bones* are never the seat of primary actinomycosis. Those most commonly invaded secondarily are the lower jaw, vertebræ, ribs, and occasionally the upper jaw and the base of the skull. They undergo extensive erosion, which is not, as a rule, associated with any great amount of new periosteal bone-formation. In a few cases, however, this has been considerable. In the spine, angular curvature has been reported; the meninges and the cord usually escape, though there may be intercostal neuralgia.

6. Although the *skin* is more often secondarily than primarily involved, numerous cases are on record in which it was the initial site of infection.

7. In the *tongue* the disease takes the form of a dense fibrous infiltration (" wooden tongue " of cattle), with or without multiple nodules and abscesses. (Plate 77, Fig. 2.) But this variety is very rare in man.

8. The *brain* may be invaded by metastatic deposits, carried to it by the blood-vessels, or, as in Ponfick's case, by spread from the cranial base. The abscesses are in the white matter, are usually multiple, and are surrounded by areas of cerebritis and meningitis. Their development may be comparatively rapid and occupy only five or six weeks.

9. The *heart and pericardium* may be invaded in thoracic actinomycosis.

Diagnosis.—The disease must be differentiated from—(*a*) Tuberculosis, especially tuberculous lymphadenitis and periadenitis. (*b*) Carcinoma. (*c*) Sarcoma. (*d*) Syphilis. (*e*) Chronic abscess (*f*) Chronic or subacute appendicitis in cæcal cases. (*g*) Chronic glanders of the skin and subcutaneous tissue. The following points will help in its differentiation :—

1. The history of great chronicity and exposure to infection.
2. The alternation of very dense infiltration with multiple semi-fluctuating areas.
3. The sinus-riddled condition, when present.
4. The gradual merging into the surrounding tissues.
5. The mottled bluish colour of the skin over the softened areas
6. The fact that the lymph-glands are not affected unless secondary pyogenetic infection has supervened.
7. The large size of the area involved compared with the small size of the tumour.
8. The character of the exudate.
9. The diagnosis is rendered certain by the discovery of the characteristic organism in the discharges or in the granulation tissue.

A method of *serum diagnosis* depending upon fixation of the complement has been employed, but the results have been variable, the negative reaction being especially unreliable It is apt to give a negative reply in mild, though definite, cases

Prognosis.—As regards life, the outlook is not so hopeless as is sometimes stated. Even untreated cases occasionally, though rarely, survive, and although the death-rate is high amongst patients subjected to treatment, a considerable number ultimately recover. The prognosis is worse if pyogenetic infection be added, if entrance into a vein and metastasis occur, if important organs become involved, or if amyloid degeneration follow as the result of infection with pyogenetic organisms Death results from exhaustion, amyloid degeneration, or spread to a vital organ. The prognosis is worse in internal than in superficial cases, and is especially bad in thoracic cases.

The local lesions may persist for years, but if treated may ultimately heal with considerable deformity.

Treatment.—Chief reliance must be placed on the administration of large doses of potassium iodide, even more than 200 gr. per diem being necessary in many cases before any therapeutic effect is seen. It may be given by mouth or by injection. The surgeon should be prepared for the pain and rise of temperature that may follow its exhibition, and should also give it in high dilution.

Mercurial injections have sometimes caused apparent improvement. Injections of iodipin (1 per cent.) have been useful in one of

my cases. Local injections of iodoform emulsion in vaselin have proved serviceable.

Wherever possible, locally, surgical measures, such as excision, or free incision and gentle curettage, must be practised.

Potassium iodide compresses have been used, but ordinary aseptic or antiseptic dressings are preferable. It is important to postpone secondary pyogenetic infection as long as possible. Washing out of the fistulæ with hydrogen peroxide is of value.

Daily local injections of potassium iodide (1 per cent.) into different parts of the lesion, as practised by Rydygier, have been followed by definite improvement.

In my experience the best treatment consists in the combination of surgical measures with the very free administration of potassium iodide both by mouth and by local injection.

If the organism present shows a preference for anaerobic conditions, free incision and the use of hydrogen peroxide are indicated.

As an adjuvant method of treatment the patient may be subjected to a course of vaccines; they are best prepared by grinding an ascertained weight of dried culture. Doses of 0·001 mg. may be used at the commencement, and may be increased gradually to 1 mg. at intervals of 7–14 days. At the same time vaccines may be given against concomitant micro-organisms, if present.

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TETANUS

By BREVET-COLONEL J. W. WEST, C.M.G., M.Ch., R.A.M.C.

Tetanus is an extremely fatal disease, due to the introduction into the tissues of the tetanus bacillus or its spore, which elaborates at the site of inoculation a toxin possessing a special selective action for nerve tissues, and producing symptoms due to an increased tone in the voluntary muscles with tonic and clonic spasms.

History.—This disease has been recognized for centuries, and also its connexion with wounds and its fatal character.

In the new-born it has at times been a very serious disease. In the West India Islands it exacted a heavy toll amongst negro children, and nearer home, in the Western Hebrides, the incidence among infants was very high until antiseptic precautions were taken to prevent infection of the cut umbilical cord.

Its occurrence in war is largely determined by the terrain of the hostilities: thus, in South Africa, where the fighting took place over virgin pasture-land, the disease scarcely existed, whereas in France and Flanders, where the country is agricultural and heavily manured, it was very prevalent. But even over areas of manured land, as was noted in Manchuria, Flanders, and East Africa, the liability to infection varied greatly.

The characters of *B. tetani* and the history of its discovery are discussed at p. 84.

In 1892 the presence of the toxin was demonstrated in the central and peripheral nervous systems, but it was not until 1901 that the work of Marie and Morax, and that of Meyer and Ransom, showed that the toxin was transferred to the central nervous system by way of the motor nerves. This path along which the toxin travels to reach the central nervous system is most important, as explaining the incubation period, and also from the point of view of treatment by antitoxin.

The earlier work which showed macroscopic and microscopic changes of an inflammatory nature in nerves near the site of a wound cannot now be accepted as satisfactory evidence of the passage of

toxin through the nerves. Further, there are no changes in the cells of the central nervous system which can be considered pathognomonic of tetanus.

Meyer and Ransom were able to show that after inoculation into the hind leg of a rabbit the toxin could be demonstrated in the sciatic nerve. They proved also that it is only motor nerves which convey the toxin, and never the sensory nerves; and further, that it actually passes by way of the axis-cylinder and not by the lymphatics of the nerve.

Marie and Morax showed that the passage of the toxin required an intact axis-cylinder, for if degeneration was set up by section of the nerve prior to inoculation of the toxin the nerve would not take up any toxin. If the section was done just before inoculation the toxin could be demonstrated in the distal but not in the proximal portion of the nerve, showing that the toxin was not carried by the nerve-capillaries but by the axis-cylinders

In 1890 Behring and Kitasato proved conclusively that, under the protection of an antitoxin, animals could enjoy an immunity against the toxins.

Habitat of the tetanus bacillus and mode of infection.—Although the bacillus of tetanus is said to exist as a saprophyte in the intestines of man, this has never been definitely proved. It is, however, constantly present in certain herbivorous animals. In horses it is almost invariably present, and in cattle if the animal is over two years old, but it may be absent from younger animals (Romer). This accounts for the prevalence of the disease in veterinary practice, and its occurrence from wounds received in the vicinity of stables. The organism is constantly present in garden earth, road dust, and manured country generally.

In surgical and medical practice, cases have been attributed to the use of imperfectly sterilized catgut (Richardson), of infected gelatin used for hæmostasis in aneurysms, and in India several cases have occurred after the subcutaneous or intramuscular injection of quinine.

The organism is probably unable under ordinary conditions to grow in the tissues of the body. *Although a strict anaerobe, it may* grow in an open wound provided there is a mixed infection present, and a certain amount of dead and necrotic tissue. The ordinary pyogenetic organisms, by using up the available oxygen, secure the conditions necessary for growth. Consequently, war wounds produced by modern high-velocity missiles, where the infection is deeply implanted and other organisms are invariably present, with areas of dead and damaged tissues and retained foreign bodies, provide an ideal breeding-ground for the tetanus bacillus. So, when hos-

tilities take place over a highly cultivated and manured country, the disease is certain to have a high incidence.

Although so-called cases of idiopathic tetanus have been described, there is, in all probability, always some breach of surface through which the bacillus gains entrance

During its growth the tetanus bacillus produces a powerful toxin. It is interesting to note that Tulloch has identified, from material taken from a tetanus case, bacilli with terminal spores, which are morphologically indistinguishable from the tetanus bacillus yet are non-pathogenetic, and from serological evidence are not the true organisms of tetanus He has, further, identified three antigenic types of tetanus bacillus Tulloch draws special attention to the way in which *Bacillus sporogenes* assists the growth of the tetanus bacillus in the tissues.

Incubation period.—In the unmodified disease, where no prophylactic dose of antitetanic serum has been administered, the incubation period is fairly constant.

In the Franco-German War of 1870-1, before the days of prophylaxis, 80 per cent. of the cases developed symptoms within a fortnight after wounding; only 20 per cent. had an incubation period of over fifteen days. In the first 180 cases treated in home hospitals during the late war, before general prophylaxis was introduced, 75 per cent. developed symptoms within fourteen days, and most of the cases occurred on the tenth day. But in some cases an incubation period of one or two days has been noted, and in others more than a month. After the introduction of universal prophylactic use of serum, the incubation period of the disease was lengthened; at the same time its type became milder and its mortality was diminished.

In the American Civil War, before prophylaxis was used, only 8·1 per cent. of American cases had a longer incubation period than twenty-five days, whereas 21·7 per cent. of British cases during the recent war occurred after that day (Cummins).

Taking a series of 1,499 cases which occurred in France and England, the largest number developed symptoms on the eleventh day, with other high peaks on the chart on the seventh, ninth, and fourteenth days, and after the fourteenth day there was a rapid fall

The time intervening between the date of infection and the initial symptoms is the time required for the toxin from the wound to travel through the motor nerves to the cells in the central nervous system; this may account for the short incubation period noted in some cases of cephalic tetanus, where the nerve-path is short.

Symptoms.—Since the prophylactic use of antitetanic serum has become so frequent in wounds where tetanus is likely to arise, a new type of the disease has been produced, and consequently there are

two separate groups of symptoms to be described—those occurring in unmodified tetanus, and those arising in a patient partially protected by serum.

Premonitory symptoms.—For successful treatment, early recognition of tetanus is most important. Unfortunately, by the time trismus, which is often the first sign, appears, the disease is fully developed and the toxin has combined with and damaged nerve-cells, and serum treatment will have lost much of its efficacy. The early observation, therefore, of premonitory symptoms is very necessary. K. Elver, who himself suffered from the disease, supplies a list of these warning signs and symptoms. They are not all necessarily present in any one case, but some of them are present in most patients who develop the disease. They include sleeplessness, and distressing dreams or delirium; difficulty in micturition due to spasm of the sphincter of the bladder; temporary giddiness, violent headache, excessive yawning; an anxious facial expression, although no risus sardonicus has as yet developed; trembling of the tongue, which may be put out to one side; profuse sweating, and darting pain in various situations; throbbing of arteries, although the limb is elevated; and slight jerking following pressure on the flexor tendons. As later premonitory symptoms, Elver mentions increased flow of saliva, reflex cramp of the œsophagus, nystagmus, strabismus, spasmodic cough, hyperacousis, tremors, and clonic spasms which are not painful and may not attract attention. To these may be added a temperamental change in the patient, with a tendency to become quarrelsome, and also severe stitch in the side.

In some cases the toxin of tetanus reaches the spinal cord primarily by the nerves which are in connexion with the seat of injury, and hence the muscles in the vicinity of the wound will first be affected by spasm ("local" tetanus). The patient may complain of stiffness or jumping of the part, and in all wounds infected with suspected material this symptom should be carefully looked for at each dressing.

These early symptoms in the neighbourhood of the wound are, however, most common in patients who have been partially protected by a prophylactic dose of serum.

Signs and symptoms of unmodified tetanus.—The onset may be heralded by chilly feelings, or by a definite rigor. But the first symptom commonly noted is trismus. The patient complains of stiffness of the jaw, or inability to open the mouth ("lockjaw"). That this is due to spasm of the masseter muscles can readily be verified by palpation of the muscles, or by introducing the finger into the mouth, when the tense anterior edge of the muscle can be felt. About the same time, or in some instances earlier, there may be stiffness and

pain at the back of the neck. Other groups of muscles then become successively affected; the recti abdominis are early noted to be tense and rigid, and next the back and lower extremities become involved. It is an interesting and important fact that the hands and forearms tend to escape. At this stage, or in some cases earlier, the muscles of deglutition become affected and the patient experiences great difficulty in swallowing. The face assumes the typical expression, which has aptly been called the risus sardonicus; the eyebrows are raised and the angles of the mouth drawn out.

As the disease progresses, the muscles which at first are simply in a condition of increased tonus become subject to paroxysmal spasms. In the earlier stages these spasms appear only on stimulation, the stimulus being often of a very trivial nature, such as a draught of cold air, a sudden noise, or a touch on the patient's bed. Later, the spasms occur without any special provocation. In severe spasms the patient may assume the most extraordinary attitudes. The powerful muscles of the back being always much affected, the most common attitude is that of opisthotonos, in which the back is arched to such a degree that the patient may be supported on his heels and the back of his head The conditions of pleurothotonos and emprosthotonos, where the patient is bent laterally and forwards respectively, also occur, but less frequently. Extreme suffering is produced by these spasms; muscles such as the recti abdominis may be torn, and actual osseous fractures have taken place.

During the seizures, owing to the spasm of the diaphragm and the intercostals, the patient is unable to breathe and feels as if held in a vice, and marked cyanosis results. The spasms are followed by profuse sweats. Swallowing becomes increasingly difficult, and, as a rule, the patient can only ingest liquids. Retention of urine and constipation occur from the increased action of the sphincters, and the attempt to pass a catheter usually precipitates a spasm. The urine is scanty, and may contain albumin or blood.

In the worst cases the spasms may occur every few minutes, but in others at half-hourly or hourly intervals. In some cases a temporary improvement is noted on the fourth day, frequently followed by relapse.

From the earliest stage of the developed disease all the reflexes, both superficial and deep, are increased. Babinski's sign can be elicited.

A most distressing feature of the disease is sleeplessness, which can be overcome only by dangerous doses of sedatives. Fever is rare and, when present, can usually be accounted for by the condition of the wound, but just before death high temperatures have been recorded. The pulse-rate is always accelerated. In many cases

death ensues in from five to seven days, the mind remaining quite clear until near the end, and the patient being fully conscious of his serious condition

Other and rarer combinations of symptoms may arise. Thus, in *wounds of the head and face* the facial nerves may be paralysed while other parts of the body are involved in spasm. Usually only one facial nerve is involved, but in association with central wounds of the head both may be affected. In wounds in the neighbourhood of the eye, oculo-motor paralysis may be the first symptom; the third nerve is most commonly involved, but the fourth and sixth may be affected as well.

The disease does not invariably assume the acute type just described, and chronic cases occur, even in unprotected subjects, where *spasms occur only at long intervals. These cases show* a tendency to relapse. When recovery takes place, stiffness and contractures of groups of muscles may persist for prolonged periods

Symptoms of modified tetanus.—This type of the disease corresponds to the experimental tetanus produced in animals by the injection of tetanus toxin. Here the spasm commences at, or may remain confined to, the site of wound or inoculation. In man this type usually occurs when partial protection has been produced by an injection of antitetanic serum, but it is not unknown in the unprotected subject. In the most favourable cases the disease may remain localized to the wounded part, but in others may pass on into the condition described under the generalized disease, and hence treatment in these cases should be carried out energetically. The patient commonly complains of pain or stiffness in the part, especially on exertion, and the spasm can be aggravated by local stimulation. The prognosis in these cases is much more favourable than in cases of descending tetanus *where the masseters are first involved.* During the late war there was no mortality from local tetanus (Bruce)

Diagnosis.—When tetanus is fully developed there is no difficulty in arriving at a correct diagnosis, but the earlier manifestations, and atypical varieties of the disease, may present many difficulties.

In war wounds, experience has led us to watch for the early signs and symptoms, but in civil practice, where the disease is not anticipated, these early premonitory symptoms are likely to escape notice.

The conditions for which tetanus is most likely to be mistaken are :—

1. *Local conditions producing spasm of the masseter* and difficulty in opening the mouth, such as affections of the parotid gland, unerupted wisdom tooth or caries of the teeth and dental abscess, *foreign* bodies lodged in the masseter muscle, *tonsillitis, arthritis* of the temporo-maxillary joint

2. *Meningitis*.—Here spasm of the neck muscles occurs, but the freedom from spasm of the masseters, and examination of the cerebro-spinal fluid obtained by lumbar puncture, will serve to distinguish the two diseases. In tetanus the cerebro-spinal fluid is clear, whereas in meningitis changes in the cellular content will be found, and if the case is one of cerebro-spinal meningitis the meningococcus can be demonstrated.

3. *Strychnine poisoning*.—Here the absence of a wound and the fact that there is complete relaxation between the spasms, which come on at once, will make the diagnosis clear

4. *Tetany*.—In this disease the attitude of the hands is characteristic, whereas in tetanus the hands and forearms tend to escape.

5. *Hydrophobia*.—The history of a bite from a rabid animal, and the fact that the individual paroxysms are distinct and affect principally the laryngeal muscles, and are followed by periods of relaxation, will be of assistance.

Bacteriological examination.—Unfortunately this is not always of much assistance. In the unspored state the bacillus is not characteristic, but although in the wound it is usually sporing, other organisms with terminal spores which are not pathogenetic may be found. Further, many war wounds contained the tetanus bacillus and yet the disease did not arise.

Causes of death.—The most common cause of death in tetanus is gradual cardiac failure, with increasing œdema of the lungs. Some patients, however, die suddenly from asphyxia during a spasm. Many die after the spasms have apparently ceased and the case looks favourable for recovery. In all such cases post-mortem examination shows that œdema of the lungs is the only pathological change.

Mortality.—Before the introduction of prophylaxis and specific treatment of the established disease by antitetanic serum the disease was very fatal. In the American War of Secession the case-mortality was 89 3 per cent. In the Franco-Prussian War of 1870–1, among the German troops it was 90 per cent.

Unfortunately, war statistics relating to the mortality of tetanus are likely to be fallacious, for many of these cases are seriously wounded men who die from septic complications such as gas gangrene and secondary hæmorrhage Figures given by Permin and Faber, from hospital cases in Denmark where these complicating factors do not arise, show a mortality of 79 per cent. During the late war a total of 2,508 British cases occurred with 1,254 deaths, giving a mortality of exactly 50 per cent.; but, excluding the early figures, from 1916 to 1919 the mortality from tetanus in France was 45·9 per cent. For the period 1918–19 it was 31·9 per cent. (Cummins). (Chart 6.)

Prognosis.—The length of the incubation period has a marked *bearing on the prognosis. If it is* under ten days the outlook is much more serious than if a longer period has elapsed. In a series of civil cases in Danish hospitals, 94·7 per cent. died when the incubation period was under ten days, and 70·2 per cent. when the incubation period exceeded that time. During the late war, *in home hospitals,* 60 per cent. died with an incubation period up to ten days, 35 per cent. when the period was eleven *to twenty-one* days, *and* 15 per cent. when the period was over twenty-two days. In France the figures were higher, due probably to the fact that the patients

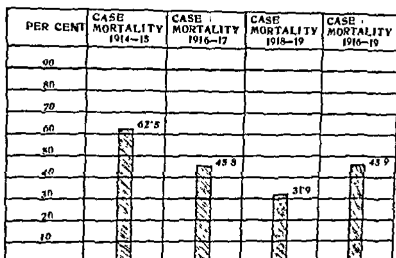


Chart 6.—To illustrate the reduction in case-mortality in tetanus during the war. (*Cummins.*)

retained there represented the most seriously wounded cases. Thus, 74 per cent. died when the incubation period was under ten days, 68·4 per cent. when the period was eleven to twenty-one days, and 43·5 per cent. when the incubation period extended beyond the twenty-first day (Cummins). One of the most pronounced effects of a prophylactic dose of serum is a lengthening of the incubation period, with a corresponding improvement in the prognosis.

The time that has elapsed since the onset of symptoms is also an element in prognosis. If the case has lasted less than ten days the chances are against the patient; after the tenth day the chances of recovery progressively increase with each day passed.

In acute cases, where successive groups of muscles become rapidly involved, the prognosis is bad; whereas in chronic cases, and in cases where the spasm remains localized, the prognosis is better. Cases *with spasm of the diaphragm* are *very fatal.* Hyperpyrexia is a bad sign.

In cases of local tetanus the prognosis is good and recovery is the rule, but some of these pass on to the generalized disease, and in consequence treatment should be prompt and thorough.

Treatment. 1. **Prophylactic.**—Prophylactic injections of anti-tetanic serum, given as soon as possible after the receipt of a wound, have undoubtedly had a pronounced effect in diminishing the incidence of tetanus. Early complete excision of the wound, with removal of all foreign bodies and dead and damaged tissues, must have been a contributing factor In gas gangrene, also due to anaerobic organisms introduced into the wound, it was found that among cases admitted to base hospitals during quiet periods on the fighting front, when every wounded man had his wounds excised and at times closed by primary suture, practically no cases of this disease occurred. It is almost certain that the incidence of tetanus was diminished in the same way. Consequently, early and efficient excision is strongly advocated for every wound in which infection with the tetanus bacillus is likely.

The Franco-Prussian War, fought before the days of prophylaxis over the same country as the late war, is suitable for comparison. In 1870–1 the Germans had an incidence of 3·5 per 1,000 wounded; in the late war the British figure was 1·52 per 1,000 wounded.

This improvement must be largely attributed to the use of prophylactic serum, and is all the more remarkable as it includes the cases which occurred in 1914, before protective doses of serum were administered. Further, the type of wound in the late war, produced in many cases by high-explosive and shrapnel shells, was much more likely to supply a suitable breeding-ground for the tetanus bacillus than the wounds sustained in the campaign of 1870–1.

In America the reduction of cases following 4th of July celebrations is a further proof of the value of prophylaxis. In 1903 the number of cases was 417, in 1914 only 3 cases occurred.

Comparing the early months of the late war, when little antitoxin was procurable, with subsequent periods, when it was available for every wounded man, we find that in the four months August, September, October, and November, 1914, with less than 200,000 men in the field, 163 cases of tetanus occurred in hospitals in England, whereas in January, February, March, and April, 1918, with 2,000,000 men engaged, we had only 90 cases. These two periods are suitable for comparison as the type of military operations was similar and both involved a retreat. The comparison favours the early period, for many of our wounded who probably developed tetanus were left in German hands and are not included in the records. (Chart 7.)

Another striking proof of the value of prophylaxis is brought

out by a study of the chart produced by Cummins *showing the incidence of the disease by months.* This presents a sharp rise in the

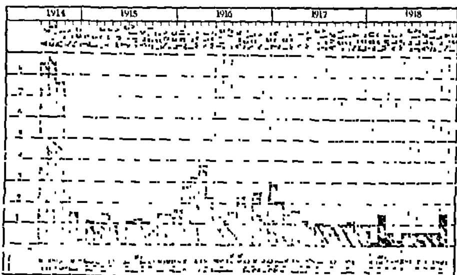


Chart 7.—Ratio per 1,000 cases of tetanus to total wounded, less gassed, in the war. (*Cummins.*)

figures for December, 1916, due to the occurrence of tetanus in cases of "trench foot." An order was at once issued that every case of "trench foot" was to receive a dose of serum as a prophylactic,

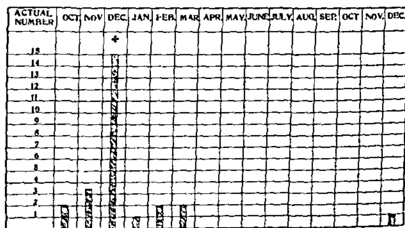


Chart 8.—To show the effect of tetanus prophylaxis in trench-foot cases in 1916-17. (*Cummins.*)

and from that date the disease practically ceased to occur in this condition (Chart 8.)

Early in 1917 another slight rise in the number of cases occurred. This was at a time when, from the nature of the hostilities, the casualty clearing stations were much on the move, and it may consequently be inferred that the rise was partly due to the absence of early and complete surgical treatment of the wound, but was probably also contributed to by the fact that, owing to pressure of work and rapid movement of the field ambulances, some of the wounded failed to receive a protective dose.

In addition to a marked lowering of the total number of cases, we have already shown (p. 921) that the prophylactic dose produced a longer incubation period, and hand in hand with this a lower mortality (p. 926). Thus, Cummins relates that among 19 wounded men who had no protective dose the mortality was 84 per cent., while during the same period 136 inoculated men developed tetanus with a mortality of 55·1 per cent.

The prophylactic used, and its dosage.—Throughout the war, except for a small batch of serum received from Paris in the early days, the standard of dosage was the U.S.A. unit, which represents ten times the least quantity of serum that is required to preserve the life of a 350-grm. guinea-pig for ninety-six hours when injected subcutaneously with the official test quantity of standard toxin. (This test quantity is 100 minimal lethal doses.)

The serum was usually supplied in phials containing 1,500 U.S.A. units in 10 c.c. of horse-serum. For treatment a concentrated serum was also supplied which contained 8,000 units in 10 c.c. There was a good deal of controversy about the dose required to protect a patient. The Tetanus Committee, presided over by Sir David Bruce, express the opinion that there is no evidence to show that 500 units was not sufficient if followed up by similar doses at seven-day intervals.

Although 500 units was the usual dose, in 1916 an order was issued in France that all cases of severe wounds, and those associated with fractures, should be given an initial dose of 1,000 units, and just before the armistice the trial of 1,500 units as a first dose was begun. This latter order came too late for its effects to be judged, but it is definitely shown that, as between 500 and 1,000 units, mortality was appreciably lower in cases which had the larger initial dose.

At first reliance was placed on a single prophylactic injection, but, as there was strong experimental evidence that the immunity derived from a dose of serum is to a large extent lost at the end of ten days, it was decided that every wounded man should receive four doses in all, to follow each other at seven-day intervals, in order to anticipate the total disappearance of antitoxin from the blood.

Charts produced by Cummins show that the case-mortality was

lower after the introduction of multiple doses; it is strongly recommended, therefore, that in large suppurating wounds where *tetanus infection is possible, at least four doses should be given at seven-day intervals.*

The danger of anaphylaxis is negligible when these doses, given subcutaneously, are contained in 3 c.c. or less of horse-serum.

The time after wounding when the serum is administered is important, and an analysis of the figures in a series of cases shows that if the inoculation was within twenty-four hours the mortality was 63·2 per cent.; if later than twenty-four hours, it rose to 76·7 per cent.

An interesting and important fact of prophylaxis is that as the serum is only an antitoxin it does not lead to the elimination of the *tetanus bacillus* from the body. A consequence of the universal prophylaxis during the war has therefore been to multiply carriers of the disease who do not appear to develop any active immunity, so that cases of tetanus have arisen after operation on old war wounds, even when healed. Consequently, it is important, before operating on such cases, to produce immunity by an injection of antitoxin given subcutaneously twenty-four hours before operation. If the operation is an urgent one, the injection should be intramuscular or intravenous.

From the foregoing considerations it is clearly the duty of the surgeon, whether in civil or in military practice, in cases where a *wound has been fouled with road dust, stable refuse, or earth from* cultivated country, to protect the patient by an injection of at least 500 U.S.A. units of tetanus antitoxin given as early as possible after the infliction of the injury. If delay has occurred before the patient comes under treatment, a larger initial dose, 1,000 to 1,500 units, should be given, and the primary inoculation should be followed up by further doses of 500 units given at seven-day intervals as long as the wound is septic.

2. **Treatment of declared tetanus.** (1) *Specific treatment.*—The value of antitoxin in the treatment of developed tetanus is by no means on the established footing which it holds in prophylaxis. Even at the end of the war, Bruce expressed doubts as to its value; while Cummins, from a detailed study of the records of tetanus cases which occurred during the war, is unable to give a definite opinion. Civil cases show better results than military cases, and this is only what would be expected. As already pointed out, the cases which occur in war are often in grievously wounded men, not seldom with multiple wounds, and death is frequently due to the severity of the wound, or to complications like gas gangrene, secondary hæmorrhage, septicæmia, etc.

Further, much controversy has arisen over the best method of administering the serum, whether by the subcutaneous, intramuscular, intravenous, or intrathecal route. While most of the statistical evidence, drawn from the returns of tetanus cases rendered during the war, is unconvincing with regard to the value of serum treatment, it is not possible to ascribe the great reduction in mortality entirely to improved surgery combined with the prophylactic dose or doses of serum; some of the improvement was probably due to the specific treatment. The clinician who was in charge of the cases was satisfied that it was of value. When we consider the results obtained in civil cases where no prophylactic was used, and the results of experiments on animals, it is clear that the patient who is suffering from tetanus must be treated with serum. Permin, in Danish hospitals, compares 199 cases not treated with serum with 189 cases that had antitoxin, the recovery-rate being 21·1 per cent. in the first group, against 42·3 per cent. in the second.

To judge of the value of treatment by serum, we must bear in mind, as indicated by Kanthack, that the disease has to be divided into three groups—the hopeless cases with a short incubation period, those mild cases with a long incubation period which recover whatever the treatment, and a small intermediate group in which alone the value of treatment can be demonstrated.

To decide rightly on the value and methods of antitoxin treatment, we must consider the conditions which exist when the disease has developed, and the experiments which have been carried out on animals. When spasm has developed in muscle, (*a*) toxin has combined with and damaged nerve-cells, (*b*) toxin is circulating in the blood and lymph-stream, (*c*) toxin is still being manufactured at the wound.

The circulating toxin can be neutralized by antitoxin given in sufficient amounts either subcutaneously, intramuscularly, or intravenously. But although toxin travels along nerves and combines with nerve-cells, antitoxin has no such power. For developed tetanus the subcutaneous and intramuscular methods are too slow, for antitoxin given by these routes requires twenty-four to forty-eight hours to reach its maximum concentration in the blood. By intravenous injection the circulating toxin can be rapidly neutralized, but here the risk of anaphylactic shock must be considered when the patient has had a previous injection of serum

The Tetanus Committee, already referred to (p. 929), did not recommend the intravenous route on account of this danger, but in such a desperate condition heroic remedies are justifiable, and it was frequently employed, after taking steps to induce anti-anaphylaxis, without any untoward symptoms arising.

It has been proved that antitoxin and drugs generally only pass very slowly from the general circulation into the cerebro-spinal fluid, which bathes the central nervous system, and consequently the method of intrathecal injection was advocated. The statistics of the late war show no reduction of mortality from the employment of this route, but there are several factors which may account for this, and individual workers, and the results of civil cases, show a pronounced improvement in results from intrathecal injections. It is, however, on the remarkable series of experiments carried out by Sherrington that we should base our judgment of this method. Even allowing for the difference between men and animals, and the fact that the symptoms were produced in animals by the injection of artificially prepared toxin, and not, as in men, by toxin elaborated by the growing bacillus, the results are so striking that no patient should be denied the benefit of intrathecal treatment. In Sherrington's experiments, toxin was injected into a series of monkeys in quantities that invariably led to death from tetanus on the fourth or fifth day, as proved by controls. After spasm had commenced, antitoxin was administered by the various routes in different series of the animals, with the following results :—

Of 25 treated by the subcutaneous method, 2 recovered.

Of 25 treated by the intramuscular method, 3 recovered.

Of 25 treated by the intravenous method, 7 recovered.

Of 25 treated by the intrathecal route, no less than 14 recovered, and in this group smaller doses of antitoxin were given.

Although antitoxin does not readily enter the cerebro-spinal fluid from the circulation, the converse does not hold good, and antitoxin injected intrathecally soon appears in the blood-stream and so helps to neutralize the circulating toxin.

The War Office Committee on Tetanus lay great stress on the importance of early treatment, and say: "Once symptoms have developed, not a moment should be lost in administering antitoxin." The value of this advice is borne out by MacConkey's experiments on animals, which showed that a dose of antitoxin sufficient to save the life of an animal, if injected at the same time as the toxin but at a different site, required to be increased 2,000 times to save the animal's life if injection was delayed twenty-four hours.

To sum up, immediate serum treatment should be instituted in every case with declared tetanus, and in order to effect as rapid a neutralization of the toxin as possible it should be given by the intrathecal, and also by the intravenous or intramuscular methods.

Further, the dosage should be large, as the best results have been obtained where large initial doses have been given. Thus, 50,000 to 100,000 units may be given during the first few days of treatment.

Intrathecally the serum is given by lumbar puncture, 10 to 20 c.c. of cerebro-spinal fluid being drawn off and a similar quantity of serum introduced. The serum should be warmed before injection, and after the inoculation is completed the foot of the bed should be raised to aid diffusion of the serum. Concentrated serum containing 8,000 units in 10 c.c. can be obtained for this purpose, and so 16,000 units can be given at a treatment. It is strongly recommended that an intravenous injection should be given at the same time, and 30,000 units is a suitable dose If given under ether anæsthesia, which is absolutely necessary for the intrathecal injection, the danger of anaphylaxis is, in my experience, much diminished. The intrathecal doses should be repeated daily for several days, and further intravenous or intramuscular doses of serum given, the doses being gradually reduced as the symptoms abate

In cases of local tetanus, where the spasm is confined to the neighbourhood of the wound, it is generally considered that less drastic methods will suffice, but even in these it is wise to employ the intrathecal route.

There should be no operative interference with the wound, at any rate before the patient has been thoroughly saturated with antitoxin, otherwise there is danger of liberating a fatal dose of toxin. Amputation is only to be recommended if it is justified by other indications

(2) *Symptomatic treatment.*—This consists in isolating the patient in a quiet, darkened room where anything likely to provoke spasm is avoided. It is usually necessary to give sedative drugs such as bromides, chloral, or morphia Morphia is the most effective, but all these drugs should be given with caution and in moderate doses. If the spasms are very violent a general anæsthetic, as ether or chloroform, may be necessary to control them As a rule, only liquids can be swallowed, and the careful, regular administration of concentrated liquid nourishment is essential

The older methods of treatment by carbolic and magnesium sulphate have been proved to be without value in the treatment of tetanus.

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HYDROPHOBIA

By LÉON CALMETTE, M.D.

Hydrophobia is a virulent disease common to all mammifers, including man. It is transmissible by accidental—e.g. bites—or by artificial inoculation of virus. This poison is present in the nervous system and in the saliva of the animal or man affected.

It has been found with variable frequency in all parts of the globe, except Australia, which up to the present has remained immune, thanks to the strict prophylactic measures which have been taken to preserve that continent from the disease.

In England it was extremely widespread at the commencement of the last century. In 1830 the surgeons of St. George's Hospital, London, verified more than 4,000 cases due to dog bites. It has been virtually exterminated in England by muzzling dogs and by the institution of strict quarantine for imported dogs. But in the United States and in Canada it is still frequent.

Symptomatic description. 1. Hydrophobia in man.—Before the appearance of characteristic symptoms of hydrophobia the patient suffers pricking sensations and pain, more or less severe, in the region of the bite Later the disease shows itself in either the convulsive or the paralytic form.

At the onset of one or the other of these forms the patient is melancholy and restless; he seeks solitude; has headache, often violent, and accompanied by hallucinations of hearing and smell. His sleep is disturbed by terrible nightmares Sometimes his depression gives place to loquacity or excessive restlessness.

From two to five days afterwards there appear difficulty in swallowing, pain, and modification of the respiratory rhythm. When the patient tries to eat or to drink he experiences an irresistible contraction of the pharynx with painful spasms. At the mere sight of liquid his jaws clench convulsively, his gaze becomes fixed, and his breathing stops for a moment. The spasms are provoked also by a sudden current of air, by a strong light, a strong odour, or an unexpected noise.

A patient affected with hydrophobia is seldom dangerous to his attendants, but he may experience a desire to bite the sheets or the hand which tries to open his mouth.

This period of excitement, interrupted by long intervals of apparent calm, lasts two or three days, when paralysis gradually ensues, or perhaps the patient falls suddenly into an asphyxial state. The paralysis lasts at the most from six to twelve hours; it leads gradually to collapse.

In cases which are paralytic from the beginning the convulsive state is very short, and paralysis at the outset attacks the muscular groups near the seat of the bite.

The duration of the disease is then generally longer, but it is exceptional if it lasts longer than six days.

2. **Hydrophobia in dogs.**—More often in dogs hydrophobia presents itself in the convulsive or raging form.

The animal is at first depressed, restless, irritable. It no longer sleeps, or perhaps its sleep is disturbed by hallucinations. If possible, it then flees from its master's house to wander in the streets, biting dogs it meets by chance, or people who try to stop it in its course. Shut up, it tears and bites all that it can find within reach, scratches the ground, and swallows the most bizarre objects, such as pieces of wood, straw, hair, etc. The voice takes a characteristic note, and in place of barking the dog emits, with nose uplifted, a series of squeaking guttural sounds. Soon swallowing becomes painful, but even then the animal tries to drink, for it is a prey to a burning thirst. It will snap at a stick or furiously attack another dog. Its gait is weak, its tongue dirty, blood-red, and hanging from its mouth. At length paralysis sets in, commencing posteriorly, gradually reaching the bulb, and ending in asphyxia.

In mute or paralytic hydrophobia, paralysis of the jaws develops at the onset and prevents the dog from biting, but its saliva is as virulent as in the raging form. This mute hydrophobia is less usual in temperate regions, but is very common in hot countries, particularly in India and Asia Minor.

Other animals capable of propagating hydrophobia by bites are the cat, horse, ox, goat, sheep, and the rodents, principally the rat and the mouse. In English medical literature, epidemics of hydrophobia are recorded among deer by Horsley, Adami, and Coppe. In 1886 an epidemic of this kind broke out in Richmond Park, and 261 animals succumbed.

Etiology.—The infection of hydrophobia can always be transmitted by inoculation of the saliva. In both men and dogs this is virulent two or three days before the appearance of the first symptoms of the disease. A dog is thus able to transmit hydrophobia although it still presents the appearance of health.

In 1881 Pasteur and his pupils established the fact that the rabic virus is also found in the brain, in the spinal cord, and in the nerves.

The bronchial mucus and the milk may be virulent, but neither the blood, the lymph, the muscular, hepatic, and splenic tissues, nor the aqueous humour of the eye, ever become infective.

The bulb of an affected animal is by preference the organ from which to obtain the virus in a pure state. Trephining, and inoculation under the dura mater of a healthy animal of a drop of bulb emulsion from a subject dead from hydrophobia, will certainly communicate hydrophobia to the healthy animal after a period of incubation which, in the case of virus obtained from a dog, seldom extends beyond fifteen days.

Inoculation of the anterior chamber of the eye with the virus is also one of the surest methods of transmitting the disease. The same is true of intramuscular injection, but an introduction into the digestive tract and the daubing of the mucosa most often remain ineffective.

Up to the present all attempts to cultivate the rabic virus by artificial means have been unsuccessful. The micro-organisms of hydrophobia belong to the group of invisible microbes. Their dimensions are so minute that they can pass through porous porcelain filters or infusorial earth (Chamberland or Berkefeld). Emulsions of rabic bulb or brain thus filtered are still virulent; heated to 50° C for ten minutes, they are no longer so.

The virulence is destroyed very rapidly by feeble antiseptic solutions (sublimate 1 per 1,000, lemon juice, creolin, sulphate of copper 10 per cent., hydrochloric acid 5 per cent.).

Light, and drying in the presence of air, have a powerful action on the virus, which, however, retains vitality for a long time in a dry vacuum (Vansteenberghe).

Pathological anatomy. **Macroscopic lesions.**—The macroscopic alterations met with in subjects dead from hydrophobia are due to the more or less prolonged suffering, but present nothing very remarkable

The cord and the brain are generally in a state of congestion, the vessels of the pia mater are dilated, and occasionally little miliary hæmorrhages even in the white substance of the brain are present.

Schaffer and Gameléia have dwelt on the frequency of centres of necrosis and softening at the bases of the anterior and posterior horns, as well as in the neighbouring white substance. Benedikt has remarked analogous alterations in the grey substance of the brain, near the olfactory lobe and Sylvian fissure.

Microscopic lesions.—The method of silver impregnation enabled Golgi to observe the form and structure of the nervous cells in the lesions now constantly recognized in rabic men and animals.

The cells of the spinal ganglia are especially vacuolated and exhibit a fatty granular degeneration. The elements of the neuroglia are

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are particularly serious. On the other hand, bites through garments are generally harmless. But an excoriation soiled by virulent saliva is sufficient to cause infection.

The great mortality due to bites in the face, in the head or hands, has long been noted. It is due to the fact that these parts are exposed and are abundantly supplied with nerves.

Incubation period.—The period of incubation which ensues between the actual time of the bite and the appearance of the first symptoms of hydrophobia rarely exceeds sixty days in man, and is hardly ever less than two weeks.

The length of the incubation period varies with the quantity of virus inoculated by the biting animal, with the place of inoculation, and with the general condition of the subject; pre-existing alcoholism, nervous defects, or any influence which tends to lower the nervous system being aggravating factors.

Passage of virus by nerves.—The rabic virus is not carried by the circulation of lymph or blood, but during the period of incubation the nerves on the path from the bite to the nervous centres are infected. It is through them and in their corresponding cells that the transmission and growth of the infectious agent takes place (Roux, Nocard).

Experimental diagnosis. — The diagnosis of hydrophobia can only be certainly established by the experimental method—that is, by demonstrating the virulence of the nervous centres of a patient or an animal dead of hydrophobia.

This test is to be made by inoculating a dog or rabbit, by the intracerebral, intra-ocular, or intramuscular route, with several drops of emulsion newly prepared by triturating a small fragment of bulb or brain in some bouillon or physiological salt solution.

The most certain method is by trephining and intracerebral inoculation under the dura mater. Hydrophobia then appears in the inoculated animal after from seven to fifteen days. Bitten persons should be subjected to the antirabic treatment without waiting for this definite result.

Prognosis and treatment.—The prognosis of manifested hydrophobia is always a fatal one. There is no disease in which the surgeon is more at a loss. Treatment can only be palliative. It consists in placing the patient in a warm room, avoiding a bright light, draughts, noises, strong smells, and anything which might provoke rabic spasms. Hypodermic injections of morphia and rectal administration of chloral are almost the only measures at our disposal. They cannot prevent death, but may make its advent less painful.

Preventive treatment.—The different methods of preventive treatment are all derived from those initiated by Pasteur in 1885 as

hypertrophied, and there are collections of leucocytes around the degenerated cells.

Nagy, in the laboratory of *Högyes at Budapest*, has shown by Nissl's method a special process of chromatolysis of which the result is the disappearance of chromatin of the cell (*Nissl's corpuscles*).

In the cerebro-spinal and sympathetic ganglia of two men dead from hydrophobia, van Gehuchten of Louvain observed lesions which he considered specific among rabic animals. They consisted of an abundant multiplication of the cells of the endothelial capsule, followed by a varying amount of destruction of nerve-cells.

These lesions are less pronounced in man than in the dog. They are *particularly noticeable in the ganglion of the vagus nerve*.

Unfortunately, their absence has been frequently noted, and, on the other hand, they may be met with in certain aged subjects among those who succumb to syphilis, typhoid fever, cancer, or other infectious diseases. They have not, therefore, any very great diagnostic value.

The discovery of the bodies described by Negri presents much more interest. These bodies (the Negri bodies) are quite characteristic intracellular formations, localized principally in the large ganglion *cell of the cornu ammonis. They are also found in the* cells of Purkinje (cerebellum), in the Gasserian ganglion, in the pons, and in the large cells of the posterior brain.

Elsewhere they are rare Negri considers them to be parasites. To demonstrate them in sections he advises that, after fixation by Zenker's fluid, Mann's stain, prepared according to the following formula, should be used :—

Solution of eosin 1 per cent.	35 c.c.
Solution of methylene-blue 1 per cent. . . .	35 c.c.
Distilled water	100 c.c.

Stain for twenty-four hours, dehydrate in sodium alcohol (absolute alcohol 30 c.c., solution of soda 1 per cent. 5 drops); *wash with* acetic water; dehydrate; mount in Canada balsam. The Negri bodies *appear as red points, or as little rings with* a clear space in the centre.

Most bacteriologists agree to-day that these cellular formations are not absolutely specific of hydrophobia, for the Negri bodies are absent from regions of the brain most rich in rabic virus, and are present in certain subjects who have succumbed to old age or different intoxications—for example, arsenic. *They seem to result from the particular* selective action of some poisons or toxins (among others that of rabic *toxin*) on the cells of the cornu ammonis or those of Purkinje.

Pathogeny.—Deep and extensive lacerations, in which the saliva of the biting animal has widely impregnated the nervous elements,

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Solution of eosin 1 per cent.	35 c c.
Solution of methylene-blue 1 per cent. . . .	35 c.c.
Distilled water	100 c.c.

Stain for twenty-four hours, *dehydrate in sodium alcohol* (absolute alcohol 30 c.c., solution of soda 1 per cent. 5 drops); wash with acetic water; dehydrate; mount in Canada balsam. The Negri bodies appear as red points, or as little rings with a clear space in the centre.

Most bacteriologists agree to-day that these cellular formations are not absolutely specific of hydrophobia, for the Negri bodies are absent from regions of the brain most rich in rabic virus, and are present in *certain subjects who have succumbed to old age* or different intoxications—for example, arsenic. They seem to result from the particular selective action of some poisons or toxins (among others that of rabic toxin) on the cells of the cornu ammonis or those of Purkinje.

Pathogeny.—Deep and extensive lacerations, in which the saliva of the biting animal has widely impregnated the nervous elements,

fixed virus. The results are quite as good. This method is also employed at Madrid and Sofia.

Recently, A. Mario has introduced into practice the use of mixtures of rabic virus and serum of sheep hypervaccinated against rabies. This process consists in injecting on three successive days, under the skin of the abdomen of the infected patient, 2 c.c. of emulsion of fresh fixed rabic virus (1 in 10) to which 4 c.c. of antirabic sheep serum has previously been added.

After the sixth day the patient is subjected to daily injections of dried cord.

While the antirabic serum alone has no preventive efficacy, it has been shown experimentally that the injection of mixed virus and serum (with excess of virus) confers a very solid immunity against hydrophobia. Since 1904 this technique has been employed with absolute success at the Pasteur Institute in Paris in the treatment of all patients who present themselves with a serious bite, but the majority of the patients are still subjected simply to the classic Pasteurian treatment.

The average mortality from hydrophobia was formerly about 15 per cent. among persons bitten in the limbs, and 80 per cent. of those bitten in the face. Since the Pasteurian preventive treatment came into use it has progressively decreased to less than 0 23 per cent.

This simple comparison of figures is sufficiently eloquent.

the result of his studies on the modification of the rabic virus by the combined action of desiccation and heat.

With his collaborators Chamberland and Roux, Pasteur showed that the virus became attenuated in passing through the organs of a monkey, whilst it was exalted by successively passing through the systems of rabbits and guinea-pigs.

After one hundred of these passages the incubation becomes fixed, and lasts only from six to seven days, instead of thirteen to sixteen days as at first. If passage through rabbits be continued, the virus preserves indefinitely the same activity.

Suspension, in flasks containing air dried by caustic potash, of fragments of the spinal cord of a rabbit which has succumbed to the inoculation of "fixed virus," at a steady temperature of 23° C, causes a gradual decrease of virulence. After five or six days an emulsion of this dried cord no longer transmits hydrophobia to animals, even by inoculation under the dura mater.

The principle of the method of immunization discovered by Pasteur is as follows: Successive inoculations of persons bitten by rabid animals with emulsions of the desiccated cord of rabid rabbits, commencing with the most attenuated, bestows on these people, during the period of incubation of hydrophobia, an immunity sufficiently strong to destroy the virus deposited in the wound by the biting animal before it reaches the central nerves.

Experimentally, this method shows perfect efficacy. Applied to man for the first time in July, 1885, it has since given such excellent results that mortality from hydrophobia in all countries where antirabic institutes exist is practically nil.

The formula of normal treatment of bitten patients consists in inoculating on the first day, under the skin of the abdomen, as soon as possible after the bite, 3 c.c. of an emulsion made with 2 to 5 mm. of cords desiccated respectively for thirteen and fourteen days. Next day the same quantity of emulsion of cords dried for eleven and twelve days is inoculated, followed by daily injection of cords of increasing virulence. Finally, two or three inoculations of the most virulent cords are made. In general, persons bitten in the limbs receive eighteen inoculations, and those bitten in the face twenty-one; some still more when the bites are particularly serious.

Favourable conditions for this treatment can be found only in an antirabic institute, because fresh emulsions of virus ought always to be employed. Such institutes now exist in many countries.

The classic Pasteurian method above described has been modified by different experimenters with a view to making it simple. Thus, Högyes employs, in place of dried cord, a very diluted fixed virus. He injects successively emulsions of 1 in 10,000 to 1 in 100 of fresh

fixed virus. The results are quite as good. This method is a employed at Madrid and Sofia.

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ANTHRAX

By PHILIP TURNER, M.S., F.R.C.S.

Etiology.—Anthrax is a disease which is caused by infection with a specific micro-organism, the *Bacillus anthracis*. The disease is essentially one which attacks animals, especially cattle, goats, sheep, horses, and mice, while the carnivora are much less susceptible. Outbreaks are rare in this country, but the disease is more common abroad, especially in the East. When it occurs in man it results from contact with the living or dead bodies, or hides, of infected animals.

B. anthracis is a rod-shaped, non-motile organism, which often grows in chains, and is remarkable for its large size (about 6–8 μ or about $\frac{1}{3000}$ inch in length), and for the readiness with which it may be identified. When growing within the tissues of a living animal it multiplies by fission, and no spores are formed. If, however, blood, or any discharge from an infected animal, be exposed to the air, small round spores are formed within the bacillus; spore-formation also occurs in artificial cultures on solid or liquid media when exposed to air. The vitality of these spores is remarkable, and under ordinary conditions they may survive for several years, remaining capable of development and of producing the disease should they reach a suitable environment. They resist the action of many antiseptics for a considerable time, but, though they can withstand the action of boiling water for a short time, they are destroyed after boiling for from fifteen to twenty minutes.

In both man and the lower animals anthrax may commence as a cutaneous lesion, or it may primarily attack the respiratory or the alimentary tract. In the former situation, in man, it is known as *malignant pustule* or *charbon*. When it attacks the respiratory tract it is known as *woolsorter's disease*, since this variety commonly occurs as the result of the inhalation of infected débris by those whose work necessitates the manipulation of the wool or hair of infected animals. In animals the disease is characterized by fever with considerable enlargement of the spleen, and it is on this account often known as "splenic fever."

Malignant pustule is the commoner form of the disease in man, and is of greater interest to the surgeon. It is

produced by direct inoculation of an abrasion of the skin with the bacillus, the infective material being, as a rule, imported hides or hair. The disease generally occurs in those who have to handle these materials, either in the raw condition, or during or after the process of preparation. Malignant pustule rarely occurs in women. In a series of 100 cases admitted into Guy's Hospital in 1896–1910, only two of the patients were women, while there were three instances in children One of these was a girl aged 11 whose mother was employed as a brushmaker, another, a boy whose father was a waterside labourer; the third, a boy who had been playing in a tan-yard and had made for himself a moustache of goat-hair which was responsible for a lesion on his lip. The occupations of the remaining 95 patients were as follows: Waterside labourers and porters working with raw hides, 58; tanners and leather-dressers, 12; carmen, 5: brushmakers, 4; greengrocers, 3; plasterers, 2; horsehair-workers, 2; butchers, 2; milkman, 1; provision merchant, 1; bookbinder, 1; horsekeeper, 1; occupation not stated, 3. Two of the patients had previously been treated for a malignant pustule, while two independent pustules were present in another. In the great majority of the cases the occupation of the patient was of such a nature as to expose him to the possibility of infection. During and since the war there have been cases of anthrax which have been attributed to the use of infected shaving-brushes. In some of them the suspected brushes were traced, and were found to have been imported from Japan. In several instances the bacilli were cultivated from the bristles.

The lesion is usually situated on some exposed part of the skin, generally the face or neck. In the above series of cases the pustule was situated on the face in 48 patients, on the neck in 41, the forearm or hand in 8, the arm in 2, and the knee in 1.

Morbid anatomy.—Post-mortem appearances vary very considerably. Usually there are extensive œdema and induration around the primary lesion. If it is situated in the neck there may be œdema of the aryteno-epiglottidean folds, fauces, and pharynx, as well as of the glottis. Some evidence of general infection, or anthracæmia, is generally found. The stomach may be œdematous and show extensive hæmorrhages in the submucous coat; but it is more usual to find a number of small petechiæ, with or without superficial ulceration of the mucous membrane. Similar lesions occur in the intestine, more commonly in the jejunum, though sometimes in the ileum or colon. Small superficial ulcers, about ½ in. in diameter, with a grey or black centre surrounded by a ring of hyperæmia, may also be found. It is unusual for the spleen to be much enlarged. The lungs are deeply congested and œdematous, and may show

hæmorrhages either into their substance or beneath the pleura There is frequently effusion into the pleural cavities, with *œdema* of the subpleural tissues and considerable enlargement of the bronchial glands. The meninges are congested, and there may be extensive



Fig. 235.—Case of malignant pustule.

hæmorrhages in the subarachnoid space or into the lateral ventricles Small hæmorrhages into the brain substance may also be present. In a case in which right-sided convulsions occurred there was found a hæmorrhage in the left corpus striatum. The kidneys may be congested and show small extravasations of blood, especially in

patients who have had albuminuria. Effusions of fluid, clear or blood-stained, may be met with in the pericardium or peritoneum as well as in the pleura. These contain the anthrax bacillus, which is found also in the various hæmorrhagic lesions, and indeed in any organ or tissue of the body.

Signs and symptoms.—The incubation period varies from a few hours to three or four days. The patient usually first notices what he considers to be a pimple, or possibly the bite of an insect; he generally suffers considerable local irritation, and scratches the affected part. Redness, swelling, and pain increase, so that advice is usually sought by the second or third day. By this time the lesion has probably the following characters, which are typical of the fully developed anthrax pustule (Fig. 235):—In size it measures from ¼ in. to 1 in. or more in diameter. In the centre is a dry, black slough, the colour being due to extravasated blood. Surrounding this is a ring of vesicles containing a clear or semipurulent fluid. Around the vesicles is a red, indurated area which gradually shades away into œdematous skin and cellular tissue In some cases, however, the black slough or vesicles may be absent, and in early cases the redness and œdema may be slight. Occasionally there is no definite pustule, but a large brawny area with much œdema, simulating an ordinary septic cellulitis. When this condition, known as *anthrax œdema*, occurs in the neck, there is serious danger that it may extend to the mediastinum, or to the larynx, where it is likely to lead to œdema of the glottis and laryngeal obstruction. Constitutional symptoms vary a good deal in severity, but headache and dizziness are usually present, and occasionally vomiting and shivering. The temperature is only slightly raised, as a rule, but may be as high as 103° F., especially in cases of anthrax œdema. The lymphatic glands which drain the affected area quickly enlarge, but, even when very large and tender, do not suppurate.

In most of the fatal cases the bacillus becomes widely diffused by the blood-stream, producing the form of septicæmia generally known as *anthracæmia. In these cases the local lesion usually has the* characters of anthrax œdema; glandular enlargement is considerable, and the constitutional symptoms are severe. The pulse becomes weak and rapid, and the temperature usually rises, occasionally as high as 105° F. Vomiting is frequent, and there may also be diarrhœa. Breathing becomes rapid and shallow, the patient grows restless and delirious, and there may be definite indications that the nervous system is involved. Thus, a patient under Davies-Colley in Guy's Hospital had right-sided convulsions, a divergent squint, and Cheyne-Stokes respiration; while a patient of Durham's had tenderness over the dorsal spinous processes, a sensation of "pins and needles" in

the limbs, paresis of the legs, and dyspnœa owing to paresis of the diaphragm and the intercostal muscles. These patients usually die in a state of coma about a week after the onset; or death may result from cardiac failure.

Diagnosis.—*When the pustule has the characteristic appearance*, and is associated with enlargement of the neighbouring lymphatic glands, the diagnosis is usually easy. The occupation of the patient helps considerably. Any unusual septic lesion in a patient working among skins or hides should arouse suspicion that it may be anthrax. *Cases of anthrax œdema may be mistaken for cellulitis*, or a pustule may be regarded as acne, a boil, a subcutaneous septic lesion, or a septic finger. Fortunately, microscopic examination of the fluid from the vesicles, or of blood from the centre of the lesion, after staining by Gram's method (in which the colour is retained), or *with methylene-blue, will readily demonstrate* the characteristic rod-shaped organisms and lead to recognition of the disease. Bacteriological verification of the diagnosis should be made in every case.

Prognosis.—The prognosis, when the pustule is seen early and *is effectively treated, is distinctly good. In the above series of 100* cases the mortality was only 9 per cent. Even when there is extensive œdema, with thrombosis of the subcutaneous veins, and severe constitutional symptoms are present, a considerable proportion of patients recover under energetic treatment. Cases of anthracæmia *are almost invariably fatal, and in pulmonary anthrax the prognosis* is very bad, though a small proportion recover.

Treatment.—The following methods of treatment are employed for the cutaneous lesion, or anthrax pustule:—

(*a*) **Excision.**—As soon as the condition has been diagnosed an *anæsthetic should be administered and the pustule freely excised*, the incision extending downwards to the deep fascia. The raw surface should be treated either with pure carbolic acid, sulphur emulsion, or the actual cautery. The wound is allowed to granulate, and when its appearance is healthy it may be skin-grafted. If there is much *œdema*, 1-in-20 carbolic lotion may be injected around the excised area. Davies-Colley found that ipecacuanha had a marked action in retarding the growth of the bacilli, and he accordingly suggested that the wounds should be dressed with powdered *ipecacuanha*, and that the de-emetized drug should be administered internally—a method which gave excellent results.

[illegible] immunized [illegible] hould [illegible] flank as soon as possible after the diagnosis has been made. Unless there

is distinct improvement, the injections should be repeated on the following day. In severe cases 10 c.c. may be injected intravenously.

It has recently been stated that when serum treatment is employed, excision is unnecessary. The results of early surgical treatment are, however, so satisfactory that both these methods of treatment should be employed together. The question has been investigated by W. H. Ogilvie and A. W. Hall, who come to the conclusion that serum treatment should be used in conjunction with excision of the pustule. They quote the following statistics of 48 cases admitted to Guy's Hospital between 1912 and 1919: Four cases were treated by serum alone, with 1 death, or a mortality of 25 per cent.; 6 cases treated by excision alone, with 1 death, or mortality 16 per cent.; 37 cases treated by excision and injection of serum, with 3 deaths, mortality 8.1 per cent.; treatment not specified in one case which was fatal. In the series of 100 cases cited above, all of which were treated by excision alone, the mortality was 9 per cent.

It may be pointed out that in a few cases which have no special treatment recovery may take place; the central slough dries and separates, leaving a granulating area which slowly cicatrizes.

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SURGICAL DISEASES CAUSED BY ANIMAL PARASITES, SNAKE-BITES, ETC.

By FRANK COLE MADDEN, O.B.E., M.D., F.R.C.S.

SCHISTOSOMIASIS

HUMAN schistosomiasis is the term applied to the pathological effects of infestation of man by three species of schistosomes, formerly known as the bilharzia worms.

The fascinating story of the worms, their development, and mode of infection may be studied in "Manson's Tropical Diseases"; only the end-results of infestation can be dealt with here.

Surgically we are only concerned with *Schistosoma hæmatobium* (*Bilharzia hæmatobia*) and *Schistosoma mansoni* (*B. mansoni*), which limit their activities almost exclusively to the genito-urinary and intestinal tracts respectively. *Schistosoma japonicum* causes no surgical complications.

URINARY SCHISTOSOMIASIS (*Schistosoma hæmatobium*)

Some four to six weeks after the entry of the infecting cercariæ into the body, toxic symptoms—irregular fever, urticaria, enlarged liver, pulmonary and intestinal irritation—which form a definite group, appear. They last ten to thirty days, and four to eight weeks later definite pathological lesions have been formed and terminal-spined ova (Fig. 236) are found in the urine.

Pathology.—The presence of worms and ova in the submucous tissues of the mucous membrane of the bladder provokes a marked irritative-protective reaction, leading to proliferation of epithelium and infiltration of the deeper tissues with round cells, many of which are eosinophiles.

The first naked-eye appearance may be groups of minute velvety hyperæmic nodules on the mucous membrane, which coalesce and form small friable elevations, sometimes topped with minute vesicles. Later these increase in size and complexity, and form either papillomas or raised plateaux.

The infiltration and swelling tend to spread throughout the whole thickness of the visceral wall, and may extend over the entire surface of the vesical mucous membrane. Scattered throughout the infected area are yellowish-brown granules, like wet sea-sand, of calcified ova;

and later, when the mucous membrane has been largely destroyed and replaced by fibrous tissue, hard, dry sandy areas are formed. Ulceration may result from the pressure of the enormous number of ova which lie in and beneath the epithelium, or from separation of the papillomas by disintegration of their bases; in the bladder or rectum it may deepen, and originate fistulæ. Associated with all or any of the above lesions there may be a diffuse fibro-cellular infiltration, not only in all the coats of the viscus, but also in the connective tissue between its peritoneal or fascial attachments. Epithelioma may



Fig. 236.—Schistosoma ovum, with calcified contents, in the urine. The shell and its end-spine are particularly well seen.

(From a photo-micrograph in the Photographic Album of the School of Medicine, Cairo.)

develop on bilharzial ulcerations, especially of the glans penis and the anus, and a form of scirrhus cancer, with groups of ova between the epithelial masses, and even more often a sarcomatous change, are sometimes found in the bladder, with secondary deposits in the heart-muscle and elsewhere.

On microscopic examination the mucous membrane is soft, swollen, and densely packed with round cells and ova; the latter are especially thick just under the covering epithelium, and, constantly escaping, are readily recognized in the excretions. The coupled worms lie in the vessels of the submucous tissue and deeper tissues, which also show fibro-cellular infiltration in varying degrees of hardness and development. *The malignant changes mentioned above may appear in the walls of the viscus and extend widely beyond it.*

The earliest **urinary symptoms** are generally referred to the **bladder**, and consist in a slight hæmaturia, first appearing with the last few drops of urine, and accompanied, sooner or later, with irritation at the neck of the bladder and along the urethra. "Irritability of the bladder" gradually becomes more severe till it merges with the other symptoms of chronic cystitis. There is, however, now an almost constant hæmaturia Ova may be found in the urine for some time before symptoms appear, and their presence remains the one confirmative diagnostic feature throughout. Many of the ova are calcified, but others are clearer and show miracidia under the higher powers of the microscope

As the disease progresses, the symptoms increase in severity, and when once sepsis is added the destructive changes throughout the whole urinary system advance apace. The urine becomes alkaline, phosphates form on abraded surfaces and become nuclei for phosphatic stones, and obstruction or even retention of urine from bilharzial masses, stones, or bloodclot may occur. Blocking of the ureteric orifices or actual disease in the ureters themselves may lead to dilated septic ureters and hydronephrosis, soon going on to pyonephrosis; or pyelitis, septic nephritis, perinephritis, septic retroperitoneal cellulitis, and general septic infection may usher in the end.

In some cases the cavity of the bladder may be almost entirely filled with a soft cheesy bilharzial tissue; in others it may be very much diminished in size, by contraction of the fibrous infiltration of the walls or by encroachment of fibrous or cancerous masses (Fig. 237) This new tissue extends well beyond the limits of the bladder into the connective tissue and muscles in all directions, and is of stony hardness. The prostate and vesiculæ seminales do not escape even in the earliest cases, and thickening of the bladder walls is a feature from the very beginning of the disease

The **diagnosis** of schistosomiasis must be suspected in every case of irritable bladder and hæmaturia in a bilharzia-infected country, and *is confirmed by microscopical examination* of the urine Marked eosinophilia is always present, and shows itself both in the blood picture and in the cellular infiltrations of the various lesions; a complement-fixation test (Fairley) has become a most valuable means of differential diagnosis. The cystoscope may reveal the earlier manifestations or show small papillomas occluding the orifices of the ureters; but as the surface of the mucous membrane becomes abraded the difficulty of securing a clear medium, owing to the constant drip of blood and the presence of débris, makes it necessary to depend upon other diagnostic methods. Thus, with the sound, roughness of the bladder-wall, masses of raised plateaux or papillomas, ridges on the posterior wall, stones, concretions, or sandy patches can all be felt, and the size of the

bladder and the condition of the viscus and its surroundings may also be ascertained. The urine varies considerably. It contains ova throughout; in the earlier stages it may remain acid and otherwise normal except for the presence of ova and of traces of blood; later it is alkaline and full of pus, blood, phosphates, débris, and ova.

The methods of diagnosis commonly used in the investigation of the urinary system must be employed to demonstrate the presence of the various secondary pathological conditions above described.

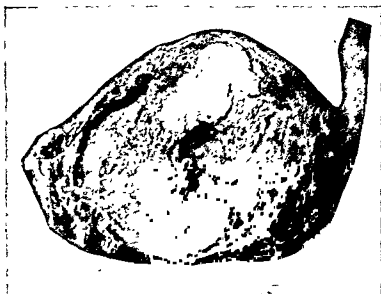


Fig. 237.—Extreme case of schistosomiasis of the bladder with formation of much dense scirrhus-like tissue. The cavity of the bladder is almost non-existent.

(*From a specimen, prepared by Professor Symmers, in the Pathological Museum of the School of Medicine, Cairo*)

Concurrently with the bladder and kidney infection, or sometimes as the main feature of the disease—which, wherever it manifests itself, must always be regarded as a general infection—the *urethra* may be involved. Infiltration of mucous membrane, followed by ulceration, with destruction of portions of the urethra and the formation of fistulæ, is the usual result. The fistulæ arise mainly from the membranous portion of the urethra, and often leave the canal laterally or even above, and run between the corpus spongiosum and the corpus cavernosum of one side, to reach the surface of the perineum, buttocks, pubes, or abdomen. In both single and multiple fistulæ there is much surrounding fibrous tissue and often a hard œdema—false elephantiasis—throughout the scrotum, perineal tissues, or

penis (Fig. 238). The penile urethra, when attacked, sometime presents extraordinary deformities produced by fistulæ and œdema, and may exude a thick, blood-stained purulent dischage from the meatus. Elongated masses of bilharzial tissue are found in the spermatic cord and in the erectile tissue of the penis, and in extreme cases the whole length of the erectile tissue may be solid with induration, and a permanent fixed erection follow. The resultant difficult

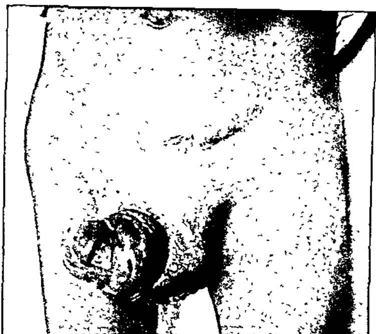


Fig. 238.—Schistosomiasis of the penis and scrotum in a young boy. The glans penis and the prepuce, indeed the whole penis, is in a condition of false elephantiasis, and riddled with sinuses, as is also the scrotum. The sinuses are really fistulæ in connexion with *extensive schistosomiasis of the urethra.* Old bilharzial sinuses are also seen in the left iliac region.

(Photograph of a case in the author's wards in Kasr-el-Ainy Hospital, Cairo)

micturition, if combined with destructive processes in the bladder, causes intense suffering.

The **treatment** of schistosomiasis consists first and foremost in a general and personal *prophylaxis*, as described in recent publications by Leiper, Fairley, and Manson-Bahr. The **symptomatic** treatment follows the usual lines adopted for irritation and inflammation of the urinary tract in general. Extract of male fern in 10-min. doses in capsule three times a day is often useful; and nothing gives more relief than the well-known buchu and hyoscyamus mixture. Other alkaline diuretics, methylene-blue, the benzoates, and hexamine, have

their value: and the acid sodium phosphate is especially useful in irritation with early alkalinity. Diuretics of various plants of local origin, and barley-water, are largely employed, and plentiful potations of water and a milk diet are sometimes urgently necessary to allay the intense suffering of the later stages. Iron and arsenic with a general tonic régime are needed also; and locally, when they can be borne, copious irrigations of the bladder with dilute solutions of permanganate of potassium, eusol, oxygen water, or even silver nitrate, may be tried. Stones must be removed by lithotrity. At a late stage, median perineal drainage of the bladder affords some degree of temporary relief. Urethral fistulæ must be very radically dealt with, and decortication of a swollen elephantiatic penis with subsequent grafting is often necessary. Sometimes an operation comparable to that for elephantiasis may be performed on the scrotum, and any malignant change on an ulceration of the glans penis may require a very complete amputation of that organ and excision of infected glands. Malignant disease arising in the bladder may call for perineal drainage, but in the later stages of the disease all these operations are purely palliative, and the whole prognosis of the case, immediate or remote, depends upon the condition of the upper urinary tract.

Deposits of bilharzial tissue in skin, subcutaneous tissue, erectile tissue of penis, spermatic cord, and elsewhere must be as completely excised as possible.

The specific treatment by the intravenous injection of tartar emetic, which originated with Christopherson, is now adopted at Kasr-el-Ainy Hospital, Cairo, where large numbers of cases are treated daily according to the scheme devised by Day. A freshly prepared 6-per-cent solution of tartar emetic in sterilized water is used, with an initial dose of 1 c c, that is, 1 gr. of the drug, which is followed by 2-gr. doses every second day for twelve injections. This constitutes a course. As Dr. Day points out, both the rapidity of effect and a permanent cure are less dependent on the total amount of the antimony given, than on a regular tri-weekly sequence of injections, which ensures an adequate saturation of the system with the drug Exceptional cases, he adds, are found in which the usual course of injections fails to kill all the ova, and more treatment is required; to discover these, it is better to examine the urine when the eleventh injection is given—instead of at the end of the course, the twelfth injection.

The urine is examined macroscopically at each injection and microscopically at the end of each course. By the end of the first week the hæmaturia has generally ceased and the number of the ova much diminished. By the end of the second week most of the ova fail to hatch out; and gradually the miracidia perish and are all dead by the end of the third week.

The *injections* are given to out-patients, the greatest care being taken to prevent either *local* or general bad effects. Slight giddiness and cough may be experienced and perhaps vertigo and headache, and in rare cases vomiting. The patients lie down for 1–2 hours after the injection. Should any local trouble arise from the tartar emetic, emetine is substituted temporarily in 2-c.c. doses of a 3-per-cent. solution in sterilized water in exactly the same way and times as the tartar emetic.



Fig. 239.—Bilharzial papillomas in the large intestine.

(From a specimen, prepared by Professor Symmers, in the Pathological Museum of the School of Medicine, Cairo.)

Colloidal antimony, in doses varying from 2 c.c., for quite small children, to 5–10 c.c. for adults, is also effective, and has the advantage that it can be given by intramuscular injection.

For the septic infections of the urinary tract which complicate so many cases of old-standing schistosomiasis, hexamine has a certain value when the urine is acid. Encouraging results follow the intravenous injections of the drug, 0.50 grm. in 2 c.c. of sterilized water, every second day, in these intense infections.

The best results are obtained in the earlier cases but considerable relief follows in more advanced cases also. Local treatment for cystitis and stone must be adopted. The excision of masses of infiltrated tissue is much facilitated by a preliminary course of tartar emetic.

INTESTINAL SCHISTOSOMIASIS (*Schistosoma mansoni*)

Toxic symptoms very similar to those described in connexion with urinary schistosomiasis occur in this form of the disease, and precede the discovery of lateral-spined ova in the fæces. The ova afford conclusive evidence of completed infestation throughout the intestinal tract and its associated viscera. The general signs of infestation in the main resemble those of *Schistosoma hæmatobium*. The Fairley reaction is equally applicable, and eosinophilia is here also a very striking feature.

Locally the disease has an extensive distribution, and bilharzial lesions have been described from the stomach to the anus (Fig. 239). A diffuse papillomatous sowing may occur throughout the mucous membrane, anywhere from the ileum to the anus, with much general infiltration. In the *colon* particularly the papillomas may separate off at their base and form ulcers not unlike those of dysentery (Fig. 240). Localized schistosomiasis may also occur in the large intestine, especially in the sigmoid, cæcum and appendix, and transverse colon, with enormous thickening of all the coats of the gut, a luxuriant papillomatous growth almost occluding its lumen, and a firm fibro-cellular induration in the mesocolon. Hard, movable swellings are produced with the usual intestinal symptoms.



Fig. 240.—Ulceration of the large intestine resulting from the sloughing off of bilharzial papillomas ("bilharzial dysentery").

(*From a specimen, prepared by Professor Symmers, in the Pathological Museum of the School of Medicine, Cairo*)

The symptoms of intestinal schistosomiasis are those of gastro-enteritis and, later, of irregular dysenteric diarrhœa with the passage of large masses of mucus and blood. The amount of blood, and its admixture with mucus, vary considerably. Bilharzia ova, with lateral spines, are found in the fæces.

Specific treatment must be adopted as for *Schistosoma hæmatobium*, but after that it becomes entirely symptomatic, and in the main follows that usually adopted for dysentery. For localized masses exploratory laparotomy is indicated, with incision into the gut at the site of the swelling; the gut and the abdominal wounds are then sutured. Great relief of symptoms, with disappearance of the tumour, generally follows.

In the *rectum* the principal features of the disease are multiple

papillomas, often in large masses, with or without protrusion (Fig. 241); *infiltration and softening of mucous* membrane, with or without prolapse; ulcerations, old or recent; fistulæ running into the ischio-rectal fossa or out on to the buttocks or sacral region; and, at the anus, hard fibrous encircling masses tunnelled with epithelium-lined tracks. Prominent masses may be ligatured off, the sphincter being stretched if necessary; ulcerated surfaces may be cauterized, or various astringents applied; while the fibrous masses may be completely removed with the lower end of the rectum.

Rarely, a diffuse papillomatous condition is found in the perineum

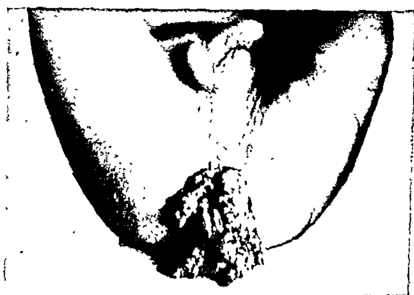


Fig. 241.—Two enormous masses of bilharzial papillomas protruding from the anus of a boy of 12. They were removed with considerable temporary relief.

(Photograph of a case in the author's wards in Kasr-el-Ainy Hospital, Cairo.)

and around the anus. Sometimes epithelioma may develop on an old ulceration at the anus

SCHISTOSOMIASIS IN OTHER PARTS

In the female generative organs, papillomas may occur at the vulva; or there may be infiltration of the mucous membrane, papillomas and ulceration at the vaginal outlet, or in the vagina; papillomas on the cervix uteri; or fibrous bilharzial masses in the broad ligament, tube, and ovary.

A bilharzial hæmoptysis is sometimes seen. Deposits appear in subcutaneous tissues, and may not infrequently be completely excised, as in the penis and perineum, or subsequently scraped and

cauterized when ulceration has supervened. A bilharzial cirrhosis of the liver is occasionally met with, and nodules on the surface of the spleen and on the parietal peritoneum. Ova may also be found in enlarged mesenteric glands. These erratic infiltrations and lesions are generally mixed infections, which are very common in endemic areas.

LESIONS PRODUCED BY THE GUINEA-WORM

The parasite.—The female worm (*Dracunculus medinensis*) is cylindrical in shape, yellowish-white in colour, and varies in length from 500 to 800 mm. or even more. Anteriorly is a triangular mouth-opening surrounded by prominent papillæ, while the posterior end is recurved on itself to form a sting or hook. The uterus extends throughout the whole length of the worm, its excretory duct opening into the œsophagus, from which the embryos are discharged. The male worm (Leiper) is only 22 mm. long; it has been found in the muscles of an infected monkey. The distribution of the worm is limited to certain tropical countries, and then only within circumscribed limits, and confined to certain sections of the population.

Symptoms of infestation.—The first sign may be a feeling of weight or a dull pain at one spot, and here a portion of the worm may be felt as a hard cord under the skin. More generally, a round, irritating lump is found in the subcutaneous tissues, over which a blister forms on the skin with much surrounding inflammation and induration. The vesicle becomes a pustule and bursts, leaving an ulcer $\frac{1}{2}$–$\frac{3}{4}$ in. in diameter, in the centre of which is a tiny opening, sometimes plugged by the head of the worm. The ulcer discharges pus and embryos. In 85 per cent. of cases it is found just above the ankle, and less commonly on the wrist or back; rarely, it may be on any other part of the skin surface, and even under the conjunctiva or in the knee-joint. There is usually only a single worm and a single ulcer, but there may be several ulcers, especially on the backs of water-carriers, or several worms may emerge from one large ulcer. General symptoms are usually insignificant, but may be very severe, with fever, œdema of hands and feet, rigors, vomiting, and delirium. Balfour and Powell have noted an eosinophilia varying from 6 to 36 per cent., and averaging 13·6 per cent. If cold water be squeezed on to the skin near the ulcer, a drop of whitish fluid jets out of the central hole; or "a beautifully pellucid tube, $\frac{1}{16}$ in. in diameter, is protruded from the opening. This is the uterus, and when it has been extruded an inch or thereabouts it suddenly fills with an opaque whitish material, ruptures, and collapses, the fluid spreading over the surface of the ulcer" (Manson). The ejection of embryos may occur almost every hour for several days until the uterus is quite empty.

Treatment.—Douching with cold water allays irritation and hastens ejection of the embryos and expulsion of the worm; as the worm protrudes it is caught in a cleft stick, or tied to it, and slowly rolled out (Fig. 242), extra turns being taken several times during the day; this may be alternated with weak antiseptic compresses during part of each day. Extraction of the whole worm may sometimes be effected in three or four days, but may take much longer. Some surgeons (Brakenridge) rely upon regular douching alone, leaving the worm to come out of itself, which it usually does in about fourteen days. Others adopt the less advisable plan of injecting the worm and its surroundings with perchloride of mercury (1 : 1,000).

Gentleness is essential to prevent breaking of the worm, an accident which may set up severe septic cellulitis, going on even to gangrene. After the extraction the long sinus usually heals without difficulty.



Fig. 242.—Guinea-worm being extracted from foot. (*From "Manson's Tropical Diseases"*)

Prophylaxis is based on the fact that the embryos must reach water for their development. They can live in clean water for six days, and in muddy water and moist earth for three weeks, but for metamorphosis into worms they must spend from three to five weeks in a small crustacean, *Cyclops quadricornis*; this is then ingested by man or other animal, and the young worms are set free. In almost exactly a year's time the female worm, having made her way along the intramuscular planes, presents herself under the skin. Impregnation probably takes place in the muscular tissues. The ulcers are usually situated on a part of the host's body most frequently exposed to the water, so necessary for the development of the embryo; thus in water-carriers the back, in other patients the legs and arms, are most often affected. Prophylaxis then consists in preventing fouling of the drinking-water by the discharge of embryos into it, and insisting upon its being boiled and filtered. Dogs, jackals, bullocks, and horses, among other animals, also suffer from infection, and must be just as carefully excluded from the water supply, which should, whenever possible, be taken from a running stream.

FILARIASIS

The **parasite** is the *Filaria bancrofti* (Fig. 243), a long, hair-like, transparent nematode worm, 3 in. to 4 in. long, the female being the larger and longer, and occupied in almost the whole length by two uterine tubes filled with ova in various stages of development. The

anterior end of both sexes is slightly tapered and club-shaped, while the tail tapers to an abruptly rounded-off tip The tail of the male, moreover, is sharply incurvated and curled. Male and female worms may be coiled together in balls, and are thus found in cyst-like dilatations of the distal lymphatics; or they may lie more loosely in lymphatic varices, in the larger lymphatic trunks between the glands, in the glands themselves, and in the thoracic duct. All the pathological conditions included in the term "filariasis" are due to the presence of these worms in the course of the lymphatic system. The embryos are non-pathogenetic, but they are of distinct importance as affording evidence of the hidden presence of the parental forms in the body.

The embryos, known as *F. nocturna* or *microfilaria bancrofti*, are slender, cylindrical worms, one end rounded off and the other tapering, 0 017 mm. ($\frac{1}{150}$ in.) long, with a diameter about equal to that of a red blood-corpuscle; each is contained in a very delicate sheath, within which it moves backwards and forwards To demonstrate the presence of *F. nocturna* in the blood, films may be examined fresh, or after staining with a weak solution of fuchsin (3 or 4 drops of a saturated alcoholic solution in 1 oz. of water), or by special methods with methylene-blue or logwood, the examination being made without a cover-glass. In fresh specimens the filariæ will be seen in very active movement among the blood-cells, and after they have quieted down they can be readily distinguished. Many films may have to be examined before any embryos are found. The examination must be carried out late in the evening; the filariæ seem to enter the peripheral circulation about 5 p m, and increase in numbers till midnight, after which they gradually decrease until about 8 or 9 a.m. the following day, when none are to be found Manson suggests that they thus wander out in the hope of being taken up by the mosquito, whose habits are also largely nocturnal, and into which they must enter to pass through the further stages of their life-history. If, however, the patient alters his habits, and sleeps during the day, the embryos are found during that time and not at night. Manson-Bahr has noted that in Fiji and the Pacific islands the embryos are found in the blood during the day, and ascribes this to the diurnal habits of *Stegomyia*



Fig. 243.—Attitudes of Filaria nocturna.
(*From "Manson's Tropical Diseases"*)

pseudo-scutellarius, the local host. During their absence from the peripheral circulation the embryos probably take refuge in the large arterial trunks, such, for example, as the internal carotid, and in the lungs. No entirely satisfactory explanation of this filarial periodicity is yet forthcoming.

Manson and others have shown that transmission from man to man occurs through the agency of *Culex fatigans*, *Anopheles nigerrimus*, and other mosquitoes, which extract the embryo with the blood from infected patients. In the mosquito the embryos undergo several changes, and pass from the stomach to the thoracic muscles and prothorax, and finally into the proboscis; thence they are injected into a new host, and reach the lymphatic system, where they become sexually mature, impregnation of the female occurs, and, in the end, ova and their contained embryos are deposited in the lymph. In due time the embryos, still contained in the stretched-out egg capsule which forms the sheath of the embryo, pass through the lymphatic glands *en route*, and enter the circulation either by way of the thoracic duct and left subclavian vein, or by the lymphatics of the upper part of the body.

Pathological effects of filariasis.—Although both adult worms and embryos are often present in large numbers without producing ill effects, they frequently do serious harm by the obstruction to lymph circulation offered by the parent worms and the ova. The lymph is dammed back and its pressure raised; thus, in time, leads to great dilatation and varicosity of the lymphatics, with lymphatic œdema or lymphorrhœa in the affected area. The obstruction may be complete from the first, as when a mass of worms or ova becomes impacted in the lumen of a lymphatic vessel; or it may be partial at first, but gradually become more complete, from inflammation and consequent thickening of the coats of the lymphatic owing to the irritation by the worms or ova within it. The ultimate effects in any case will depend upon the efficiency of the collateral circulation. Thus, if the thoracic duct itself become blocked, the chyle can only reach the circulation by passing backwards, by way of the abdominal and pelvic lymphatics, to the lymphatics of the groin and scrotum, and on by those of the abdominal wall, chest, and neck, into the right main lymphatic trunk and so to the subclavian vein. The whole of this tract of lymphatic vessels and the thoracic duct itself up to the actual obstruction may become hypertrophied, varicose, and greatly distended with chyle, which may leak from the vessels on the slightest injury, or may even exude without any breach of surface. The conditions produced, therefore, depend upon the position of the block in the lymphatic system, the degree of obstruction, and the state of the collateral channels.

Possibly some of the symptoms may be ascribed to ova obstructing the circulation through the lymphatic glands.

F. nocturna is seldom found in the blood in cases of well-developed filariasis, and least of all in elephantiasis. This is due either to the death of the parent worms (which, by their irritation, may sometimes set up abscesses or lymphangitis) or to the obstruction in the lymphatic area becoming so complete that the embryos cannot pass into the general circulation.

Clinical manifestations of filariasis. Filarial abscess.—Abscesses, particularly about the scrotum, may occur as a result of filariasis, and may sometimes be the first indication of the condition. In some cases they are due to the death of the parent worm, which may be found entire in the cavity of the abscess, or in pieces incorporated with the substance of its wall. Manson-Bahr states that adult filariæ may occur in large numbers in the tissues, especially in lymphatic glands and vessels, but also in the epididymis, testis, and tunica vaginalis, and may cause abscesses in these situations. The dead worm may, however, in many cases be entirely absorbed without producing any irritation. Most filarial abscesses are produced by lymphangitis which has suppurated, the process being comparable with that of an ordinary septic lymphangitis which ends in pus-formation.

Maxwell divides these abscesses into three main groups, according to their situation, as follows:—

1. In the scrotum, where they may occur as (*a*) suppurating hydroceles; (*b*) abscess of the spermatic cord; or (*c*) abscess below the testicle.

2. In the limbs, occurring in situations rich in lymphatic tissue, and generally in the immediate neighbourhood of the great vessels. They are particularly common in the axilla and the popliteal space.

3. Intrathoracic and intra-abdominal abscesses The former develop in the posterior mediastinum, and cannot be at all easily diagnosed. The latter are most common in the retroperitoneal tissue, especially in the iliac region. In these cases, according to Manson, there may be deep-seated pain in the thorax or abdomen with a hectic temperature and the ordinary signs of abscesses, so far as they can show themselves, and with a very marked diminution in the number of embryos or even their complete disappearance from the blood.

The condition sets in with a prolonged rigor, folowed by a high temperature in a filarial subject. Sometimes this may be associated with or preceded by an attack of lymphangitis, which usually is the precursor either of an abscess or of elephantiasis.

The *treatment* naturally consists in free incision and drainage, whenever possible.

Lymphangitis and elephantoid fever.—At any stage inflammation of lymphatic tracks may develop, possibly due to a sudden outpouring of microfilariæ by the adult worms into the tissues, these embryos producing toxic and inflammatory effects (Manson-Bahr). Signs similar to those of septic lymphangitis are present in a marked degree. Fever is high and usually preceded by a *prolonged* rigor; inflammation and induration along the lymphatics, and redness and congestion of the skin are prominent features. Abscess-formation may occur, or relief may be gained by the discharge of lymph from the surface of the swollen skin. Recovery is incomplete, for some thickening of the lymphatics and induration of the skin persists, which, increased by each subsequent attack, finally induces well-developed elephantiasis.

The attacks of fever and lymphangitis are particularly common in elephantiasis, lymph scrotum, and varicose groin-glands. If it is known that the patient has filarial embryos in his blood the diagnosis of these recurrent attacks of fever is very obvious.

Treatment must follow the usual lines for lymphangitis of other origin; special care must be taken, by massage and bandaging, to promote the absorption of the inflammatory products.

Elephantiasis of the scrotum and penis.—Elephantiasis is by far the most common manifestation of filariasis, and is very prevalent in filarial countries, especially in Cochin-China and Samoa. It has a special predilection for certain sites, such as the scrotum and the lower extremities, but it is also met with in the arms, breasts, vulva, scalp, and in circumscribed skin areas in the limbs, trunk, and neck.

It is a natural result of blocking of the lymph-stream, the first symptoms being usually ushered in by an attack of fever and lymphangitis. If the obstruction is sufficiently localized to shut out the scrotum from the lymph circulation, there will be, first, some general enlargement; the scrotum will seem more pendulous and the skin too abundant, generally softened and thickened, and either quite smooth or dotted over with tiny vesicles distended with or discharging lymph. Sooner or later an attack of lymphangitis occurs, which, after subsiding, leaves the scrotum much larger and the skin much tougher and thicker. Increasing in size with each attack, the scrotum may assume enormous proportions (Fig. 244), weights as much as 224 lb. being reported. As the scrotal swelling enlarges it drags with it the skin of the lower part of the abdomen and as much loose skin as possible from the perineum, buttocks, and thighs. The penis, which remains firmly attached to the symphysis pubis by its suspensory ligament, is dragged to an enormous length; the prepuce and the skin of the body of the organ being pulled down to form an elongated hood,

which becomes buried in the mass as a long funnel, in the depths of which is the glans penis with the orifice of the urethra. In a mode-



Fig. 244.—Elephantiasis of scrotum—ulcerated—and of legs.
(Photograph of a case in the author's wards in Kasr-el Ainy Hospital, Cairo.)

rately severe case the enlargement of the scrotum is equally distributed over its whole surface, and about halfway down the anterior

surface of the swelling the depression, the external opening of the funnel just mentioned, presents. No trace of penis or of spermatic cords is seen, nor can they be felt, in the mass. The skin is thick and rough, does not pit on pressure, and appears very like coarse pig-skin, the hair-follicles, often much hypertrophied, standing out prominently at a considerable distance from each other, and usually tipped with thick, twisted, bristly hairs, though sometimes the scrotum is quite bald. The consistence of the mass, as a whole, is soft, though the lower part is frequently harder and more prominent than the rest owing to thickening of the gubernaculum testis and to passive congestion at the bottom of the swelling. The prominence is due in some instances to hydroceles. Single or double inguinal hernia may be present also. Sometimes the scrotum alone is affected, the penis remaining quite free, but in the majority of cases of any severity the penis becomes involved in the growing mass.

When the penis alone is affected, the disease shows itself first in the prepuce, which becomes swollen and softened, and forms a horn-like projection, or a swollen collar all round the glans penis. In time the skin of the body of the penis becomes affected also, and a very characteristic appearance is produced. The body of the penis itself, including the glans, is not affected, and in all cases it can be dissected out quite intact from the infiltrated skin around it, even when it lies in the midst of an enormous scrotal swelling.

On section it will be seen that the skin layer, with all its contents, is enormously hypertrophied, and that the rest of the section consists of a mass of blubbery, fatty areolar and loose connective tissue containing many large blood-vessels. The penis, cords, and testicles are all embedded in this milky-white tissue, which can be entirely stripped from them by careful separation in the line of cleavage. The spermatic cords are enormously lengthened, and a deposit of fatty tissue runs up between the vessels in advanced cases, though, usually, there is a definite fibrous sheath enclosing the structures of the cord, which are not infiltrated generally though they are much thickened. The vessels are very much increased in size and lengthened. The testicles are soft, sometimes much atrophied, but in most cases quite healthy, and are often surrounded by large, thick-walled vaginal hydroceles containing clear fluid, not lymph or chyle.

Treatment.—These swellings, however large, are not dangerous, but become very inconvenient from their great weight and the dragging on adjacent tissues. Complete amputation affords the only hope of cure, and should be carried out when the patient's general condition permits. When the penis alone is affected, all the soft elephantiatic skin and tissue must be most completely removed, the raw surface being subsequently skin-grafted by Thiersch's method.

In cases involving the scrotum, and in which the penis is entirely hidden, the mass must be freely incised from well above the symphysis pubis to the opening of the preputial funnel, and the enormous penis and the spermatic cords, up to the external ring, cleanly enucleated, the thickened gubernacula being divided below in order to free the cords. The penis, the cords, and the testes in their tunicæ vaginales are turned up on to the abdomen out of harm's way, the urethra is guarded by a catheter placed in it, and the mass amputated. Every particle of diseased skin and subcutaneous tissue is then dissected away and the muscles are laid bare. The flaps of healthy skin that remain are undercut to form a pouch for the testes. The cords and tunicæ are now cleared of disease by careful dissection, and the testicles placed in the pouch made for them. Generally most of the penis is left bare and is subsequently grafted.

If only the scrotum is affected the operation is much easier, the cords and testicles being first dissected out, and the mass then removed as described above.

Elephantiasis of the legs (Fig. 245) is common, and is most usual below the knee, but may develop to any extent until the whole of one or both lower extremities is affected. There is a great increase in size, and the skin has the usual elephantiatic characters: the nails are rough, thick, and deformed, and around the joints deep folds are produced so that the articular movements are still possible. Usually, however, from the weight of the part and its unwieldiness, walking is exceedingly difficult if not altogether impossible, and, as repeated attacks of lymphangitis and elephantoid fever may supervene, the swelling goes on increasing till the limb assumes enormous proportions.

Treatment is, on the whole, unsatisfactory, but Castellani has reported good results from injections of fibrolysin and firm bandaging and subsequent excision of large pieces of skin. Whatever success I have had with these cases has been by *Kondoleon's operation*, which consists in making long incisions through the skin and then removing a broad strip of the subcutaneous tissues, including the deep fascia and the fascial coverings of the muscles, so as to expose a large area of muscle. Presumably a new absorptive lymph area is thus opened up and a modified collateral circulation established. The skin is then sutured and the limb elevated till healing is complete. Several strips may be removed from different surfaces of the leg and foot at different times. In extreme cases with much disability amputation may be practised. Radium has also proved beneficial in certain cases of severe lymphatic obstruction. Lymphangioplasty has, in my hands, been only temporarily successful. Streptococcal vaccines may also be tried, especially when attacks of elephantoid fever still tend to recur.



Fig. 245.—Elephantiasis of legs.

(Photograph of a case in the author's wards in Kasr-el-Ainy Hospital, Cairo.)

Elephantiasis also occurs in the arms to some extent, and in the scalp, breasts, and vulva, and may occur as pedunculated masses depending from the groins, thighs, neck, and other parts of the skin surface. Removal by free excision must be adopted whenever it is possible in these cases. A condition known as *false elephantiasis* is sometimes found in the scrotum in cases of multiple urethral fistulæ, especially in schistosomiasis, or in the limbs, particularly the legs, in cases of chronic inflammation. This latter depends often on some deep necrosis of bone in the limbs and in other places, but has nothing to do with filariasis. A careful examination for thickening of bone, openings of fistulæ, etc., must be made before diagnosis.

Varicose lymph-glands.—This condition is described by Manson as occurring particularly in the inguinal and the femoral glands and, rarely, in the axilla. They form at first painless, soft swellings, varying considerably in size, and affecting one or both groins both above and below Poupart's ligament. After a time an attack of lymphangitis occurs and the swellings become tender and increase in size. They contain a chylous or a lymph-like fluid, in which living embryos may be found. They are often associated with lymph scrotum, more rarely with chyluria and chylous hydrocele; and, on dissection, are found to consist very largely of masses of varicose lymphatics connected with a large lymphatic varix in the pelvis and abdomen. These glands should only be removed if they are causing troublesome symptoms, such as those of lymphangitis; as, in their removal, a portion of the lymphatic collateral circulation is interfered with, their excision may be followed by lymphorrhœa, by elephantiasis of the legs, or by enlarged dilated lymphatics in other parts.

Lymph scrotum is a condition, due to filariasis, in which the scrotum is enlarged and pendulous. The skin is soft and smooth, and may contain some dilated lymphatics from which lymph or a chylous fluid may escape. It is often associated with varicose groin-glands, and not infrequently becomes subject to attacks of lymphangitis and elephantoid fever, which lead to its enlargement and subsequent transformation into a typical elephantiasis. Abscess also may occur.

Treatment.—When necessary, a complete removal of the scrotum should be carried out; but this operation sometimes leads eventually to elephantiasis of the leg, or some other filarial lesion, owing to the removal of the portion of the collateral circulation.

Chylous hydrocele and filarial orchitis.—In certain cases, from the rupture of a dilated lymphatic in the wall of the tunica vaginalis, a hydrocele is formed which contains chyle. This will be painless and not translucent, and will often be associated with lymph scrotum, varicose groin-glands, or some other filarial lesion. Embryos

will be present in the blood and also, in large quantity, in the hydrocele fluid. Such cases may be treated just as simple hydroceles by periodical tappings, as there is some risk of the occurrence of elephantiasis in adjacent parts if radical operation is done. The majority of hydroceles found in scrotal elephantiasis *contain a clear fluid*, neither lymph nor chyle.

Orchitis of filarial origin is also reported, but presents *no special* features.

Lymphatic varicocele is a condition of filariasis in which the lymphatics of the spermatic cord are greatly enlarged, varicose, and tortuous, with symptoms resembling those of varicocele and requiring similar operative treatment.

Filarial synovitis, especially of the knee, is described by Maitland. At various parts of the body prominent **dilated lymphatic varices** may be met with, and sometimes in them the parent worm may be found. Similarly, **thickened lymphatics** may persist after an attack of filarial lymphangitis on the skin surface or in the subcutaneous tissues.

Chyluria, *per se,* is rather of medical than of surgical interest, and, strangely enough, it is not often associated with other filarial lesions. When, from obstruction in the thoracic duct, or in the main trunks near it, the abdominal and pelvic lymphatics become varicose, great bunches of dilated lymphatics surround the whole course of the urinary tract. If, from any cause, rupture of a lymphatic occurs, chyle escapes into the tract and will be passed in the urine. The passage of milky urine, perhaps preceded by some lumbar pain, or sometimes by retention of urine from the coagulation of the chyle in the bladder, is the first indication of the disease. The urine is subsequently passed in thin, worm-like clots, often after severe pain and distress. In either case the urine is milky, and at times may become blood-tinged; at other times it may be quite watery. The chyluria may be remittent.

The course and prognosis of a case of chyluria are very uncertain. Sometimes it all clears up, only to return after a long interval, and to disappear again as unexpectedly as before. Continued chyluria causes severe anæmia and debility. It may come on for the first time during pregnancy, or be aggravated by this condition as further ruptures of the dilated pelvic lymphatics take place. Violent exercise of any sort is also credited with inducing an attack, but usually no certain cause can be discovered.

The *treatment* resolves itself into rest and elevation of the pelvis and the lower part of the body, to assist the collateral lymphatic circulation as much as possible. The diet must be restricted, but as much fatty food given as can be borne. Malt and cod-liver oil is

given also, and good results are credited to ichthyol. Beyond this, and attention to the general health and to the bowels and other excretory organs, no treatment is of any real benefit.

Should rupture of a dilated lymphatic varix take place into the peritoneal cavity, **chylous ascites** occurs. This is usually first diagnosed by exploration. In all respects such a case must be treated as any other ascites. In one case under my observation the peritoneum contained milky fluid, in which Looss discovered the protozoan parasite *Leydinia gemmipara*, the occurrence of which and its faculty of producing milky ascites must be remembered.

Again, should a rupture occur into the lumen of the intestine in any part, **chylous diarrhœa** will ensue and will persist as long as the opening remains patent.

SNAKE BITES AND SCORPION STINGS

From a surgical point of view **snake bites** may be taken collectively and considered in order of their severity. The prognosis depends upon the dose of venom injected with the bite, its relative toxicity, the site of injection, and the age and power of resistance of the individual bitten.

1. The bite may be almost immediately fatal, from paralysis of respiration and of the heart, when an overpowering dose of very toxic venom is injected, as may happen in cobra or krait bite. If by chance the venom is injected directly into a vein, it leads to a general thrombosis, vomiting, collapse, and death.

2. The outlook in most cases, however, is not so entirely hopeless. Thus, in the case of viper bites—Russell's viper, the rattlesnake, the Australian tiger-snake, the Egyptian horned viper—there is usually an intense burning pain around the two punctures of the bite, and local redness, with a rapidly spreading œdema, often almost purple in colour and patchy with extravasated blood. The swelling may extend up the whole limb, even on to the trunk. The victim is usually in a state of terror, and may be suffering from severe shock; he becomes faint and dizzy, and finds himself unable to stand He may suffer from profuse salivation and paralysis of the muscles of the tongue and larynx, and is soon attacked by paralysis beginning in the legs but rapidly becoming general. Nausea and vomiting precede a gradual failure of respiration. Finally the heart stops, and the patient dies, with slight convulsions, in from three to fifteen hours. Recovery may occur, however, and is usually rapid and complete, though death may supervene later from septic absorption from the bite, which in all cases is infected and heals but slowly, perhaps leaving ulcerated areas.

Treatment must be prompt and thorough. An elastic ligature, or several, must be placed above the bite, and a large area around it excised (in the case of a finger or toe, immediate amputation may be done); 20–30 c.c. of fresh 1-per-cent. solution of calcium chloride is then injected, and the raw surface freely washed with a large quantity of sodium hypochlorite or calcium chloride, or rubbed with permanganate of potassium crystals. The appropriate antivenene, if available, must be repeatedly injected, and subsequently the wound must be treated *secundum artem*. To counteract shock, strychnine must be injected hypodermically in large and repeated doses, and brandy, ether and ammonia, and other forms of stimulant, vigorously exhibited. In the severest cases artificial respiration may tide the victim over his crisis.

3. In the case of bites from vipers in Great Britain, very serious symptoms may be produced, but they are comparatively rarely fatal. The symptoms come on very rapidly, with pain, redness, and swelling in the bite, extreme prostration, fainting and collapse, and even death from heart-failure. The local signs and general symptoms resemble those described above, but in a much milder degree, and treatment follows the same general lines.

4. Bites from non-poisonous snakes often produce grave symptoms of fright and shock, and sometimes violent delirium, but this symptom is more frequently ascribable to the large quantities of brandy administered by misguided friends.

Scorpion stings produce effects varying considerably with the age of the victim. They are very dangerous and quite often fatal in children, but comparatively harmless in healthy adults. When a child is stung the local signs may be quite insignificant, a tiny mark like a flea bite being sometimes seen, though, in a dark skin, this may quite escape detection. Very shortly afterwards the child faints, and may remain in a state of collapse for two or three hours, and then recover and appear to be quite well, only to have a second attack of collapse a few hours later which may progress to unconsciousness and death. In other children, and generally also in older patients, the local symptoms of pain, tightness, formication, redness, and a rapidly spreading purply œdema may be present, with varying degrees of shock, delirium, or collapse. Profuse perspiration and salivation are common signs also. Irregular muscular contractions of the limbs may occur, and even trismus, and gastro-intestinal symptoms not unlike those of irritant poisoning. Occasionally respiratory symptoms develop, and the patient dies from asphyxia or pneumonia.

Treatment follows the general lines of snake bite, with repeated injections of Todd's antiscorpion venene.

INSECT BITES AND STINGS—MYIASIS

Considerable local inflammation and general poisoning may occur as the result of bites of various insects possessing poisonous secretions, the local effects varying from a slight red irritating point to severe phlegmonous inflammation or extensive œdema. The sting of the **bee** is barbed, and is left in the wound. There is immediate intense burning pain and throbbing, rapidly followed by mottled redness and swelling which, in soft parts, may be considerable. Severe general symptoms may sometimes occur, even to fatal syncope or death from fright; and erysipelas, phlebitis, and other septic changes may result from the sting. **Wasps** and **hornets** may produce somewhat similar effects, but the sting is not barbed, and several punctures may be made close together. A general urticaria may follow these stings. The Egyptian hornet (Arabic, *dabboor*) produces very severe symptoms also, with intense pain in the bite, and a very hard œdematous swelling for a considerable area around.

Treatment.—In all such cases the sting, if left in the wound, must be removed, and alkaline fomentations applied and constantly renewed. Bicarbonate of soda and ammonia are the most efficacious, and, later, hazeline applications are most soothing. In cases of severe œdema, hot alkaline fomentations or antiphlogistin can be recommended. General symptoms may also require attention.

Spiders, tarantulas, and **centipedes** may all give dangerous bites, which may end in erysipelas or other septic conditions; and **mosquitoes, bugs, gnats, midges, ticks,** and various flies, quite apart from their danger as transmitters of specific diseases, may cause very irritating bites which, in themselves, or by subsequent contamination, may lead to serious consequences. Mosquito bites may form small blood-blisters which may suppurate and lead to a general furunculosis with all its possible dangers.

The **treatment** of all these plagues is unsatisfactory; but, in general, alkaline or hazeline lotions are the best, while, later, eau de Cologne and other spirituous applications may be tried. The intense irritation and the urticarial condition sometimes found may be relieved by calcium lactate internally, and general furunculosis yields best to an appropriate vaccine.

Bot-flies, gad-flies, and others of their nature may lay their eggs under the skin and give rise to a boil-like swelling, which may ultimately become an abscess or end in ulceration. The *ver du cayor,* the larval form of the *Ochryomyia anthropophaga* (E Blanchard) of Senegambia, and the *ver macaque,* the larva of a gad-fly, *Dermatobia cyaniventris* (Macquart), of Central America, Mexico, and Brazil, are two well-known examples of such larval infections; but much more

serious effects are produced by the wanderings of the *screw-worm*, the larval form of a blue-bottle fly known as *Chrysomyia macellaria* (Fabricius), which is found in South and North America; similar flies in parts of China and India also attack the same places. The eggs may be deposited in the skin or in the mucous membrane of the nose or skin of the auditory canal. The larvæ, on being hatched, may set up some local furunculosis in the skin, or may bore from the nose or ear deeply into surrounding tissues, even through muscles and cartilage, to the bones. In their course they may set up septicæmia, or even penetrate to the meninges and brain, with fatal consequences. More often the frontal and other sinuses in connexion with the nasal passages may be involved.

Treatment.—Extensive operations for the evacuation of the larvæ and pus may be required, with the subsequent application of strong antiseptics, such as pure carbolic or benzine. The inhalation of chloroform may be employed also to kill the larvæ (MacLeod).

Wounds may at any time become infected with **maggots**, the *larvæ of various flies, particularly in tropical countries among native* patients. Radical measures must be taken to remove such foreign *bodies and prevent their reappearance.*

The impregnated female **chigger** or sand-flea (*Dermatophilus penetrans*), *which inhabits warm, dry, sandy soil in many tropical and sub*-tropical climates, produces local irritation by entering through the soft skin, especially in the sole, between the toes, around the nails, or through any small abrasion. There may be no symptom of penetration, but usually an acute irritation with intense itching is present. At first only a tiny black spot, the posterior end of the flea, can be seen, but this soon increases in size, as the body becomes swollen with ova, until it may be as large as a pea. Inflammation and secondary suppuration occur in the surrounding tissues and may expel the flea. Dirty discharging sinuses or deep ulcerated wounds may be produced, and erysipelas, gangrene, or even tetanus may supervene. If the worm is burst within the skin, ova may be discharged from the sinus for some time, with constant irritation, or the flea may die and act as a foreign body.

The **diagnosis** in a country where the disease is endemic is easy, and the extraction of the flea *itself is conclusive evidence.*

Treatment.—The affected area should be soaked in hot soda solution *for some hours (Black), the small external opening en*larged with a fine-bladed scalpel or needle, and the flea removed —*if possible without injuring it* or spilling its contents. Antiseptic applications and dressings should be employed till the sinuses have healed. Toes may require to be amputated in severe cases, and

gangrene or deep septic infiltration must be dealt with as occasion demands.

Prophylaxis must consist in brushing the floors, anointing the feet with various strong-smelling antiseptics and parasiticidal applications, and carefully examining them daily. Leather shoes or sandals should be worn, and the floors may be kept wet with carbolic lotion or petroleum to prevent the development of the ova.

POISON WOUNDS INFLICTED BY FISH

In addition to the well-recognized symptoms of poisoning resulting from the eating of certain fish, and particularly shell-fish, either fresh or partially putrid, and the risks of contracting a specific disease, as in the case of typhoid from infected oysters, quite severe and dangerous wounds may be caused by contact with some of the hard-skinned fishes, which are armed with sharp, sometimes barbed, spines in different situations. Some of these fish, such as the sting-rays—stingaree—the Scorpœnidæ, certain of the cat-fish tribe (Siluridæ), the weavers, and others, inflict wounds comparable to those of a poisoned arrow, the spines being coated with a peculiarly irritating mucus derived from the surface of the skin. Others, amongst which may be mentioned the *Synanceæ verrucosa* and *horrida* and the Thalassophryna, possess definite poison sacs at the base of deeply grooved spines. The venom is injected by pressure, and, if in sufficient quantity, may produce very dangerous general poisoning effects, or even death

Speaking generally, jagged, irregular wounds result which are often intensely painful and are almost invariably followed by considerable swelling, lymphangitis, cellulitis, or gangrene. All the possibilities of general septic absorption are also present. The direct effect depends entirely upon the nature and quantity of the poisonous material injected; in severe cases delirium, convulsions, and death may follow.

Treatment, both local and general, must be conducted on the usual principles for poison wounds. Whenever possible a ligature should be applied above, the wounds enlarged and allowed to bleed freely, and then cauterized with pure carbolic, permanganate of potassium, turpentine, or other strong antiseptic, and dressed with antiseptic fomentations. Iodine may be applied to the wounds in other cases.

The dangers arising from the ingestion of fish which are acting as hosts to some developing parasite (*Bothriocephalus latus* in certain fishes, hydatids in congers), and the effects produced by electric eels and fishes (torpedo fish), can only be mentioned.

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